569. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable non-radioactively labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactively modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more detectable non-radioactively modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

subjecting said detectable non-radioactively labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively the presence of each of said separated or resolved fragments by means of said detectable non-radioactively modified or labeled nucleotides or nucleotide analogs, and determining the sequence of said nucleic acid of interest.

570. (NEW) The process according to claim 569, wherein the nucleic acid sequence of interest is derived from an organism.

571. (NEW) The process according to claim 570, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing.

572. (NEW) The process according to claim 571, wherein said organism comprises a mammal.

573. (NEW) The process according to claim 572, wherein said mammal comprises a human being.

574. (NEW) The process according to claim 570, wherein said organism is living.

575. (NEW) The process according to claims 570 or 574, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes.

576. (NEW) The process according to claim 575, wherein said organism comprises a eukaryote.

577. (NEW) The process according to claim 576, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome.

578. (NEW) The process according to claim 576, wherein said eukaryote comprises a mammal.

579. (NEW) The process according to claim 578, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome.

580. (NEW) The process according to claim 578, wherein said mammal comprises a human being.

581. (NEW) The process according to claim 580, wherein said human nucleic acid sequence of interest is contained within a chromosome.

582. (NEW) The process according to claim 581, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library.

583. (Amended) The process according to claim 569, wherein in said providing or generating step the fragments are provided or generated by one or more primers, nucleoside triphosphates or analogs thereof, or a combination thereof.

584. (NEW) The process according to claim 583, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing.

585. (NEW) The process according to claim 569, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

586. (Twice Amended) The process according to claim 569, wherein the detectable non-radioactively labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

587. (Amended) The process according to claim 569, wherein said providing or generating step, the one or more non-radioactively modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments.

588. (Amended) The process according to claim 587, wherein at least one of said non-radioactively modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments.

589. (NEW) The process according to claim 588, wherein said terminus comprises the 5' or the 3' terminus.

590. (NEW) The process according to claim 587, wherein said incorporation has been carried out in the presence of a primer.

591. (NEW) The process according to claim 569, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme.

592. (NEW) The process according to claim 591, wherein said enzyme comprises terminal transferase.

593. (NEW) The process according to claim 569, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling.

594. (Wholly Rewritten) The process according to claim 593, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

595. (NEW) The process according to claim 593, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase.

597. (NEW) The process according to claim 569 or 596, wherein said incorporation is carried out by means of a polymerizing enzyme.

598. (NEW) The process according to claim 597, wherein said polymerizing enzyme comprises a polymerase.

599. (NEW) The process according to claim 598, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase.

600. (Amended) The process according to claim 569, wherein said providing or generating step, the non-radioactively modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

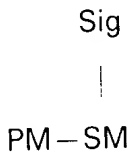
BASE is a pyrimidine, a purine or a 7-deazapurine base moiety or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof,

at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

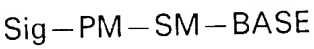
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

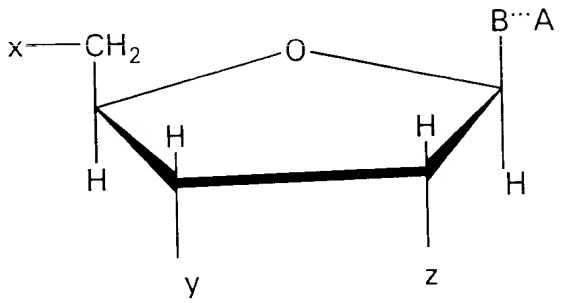
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

601. (Amended) The process according to claim 569, wherein said providing or generating step, the non-radioactively modified or labeled nucleotides or nucleotide analogs have the structure:



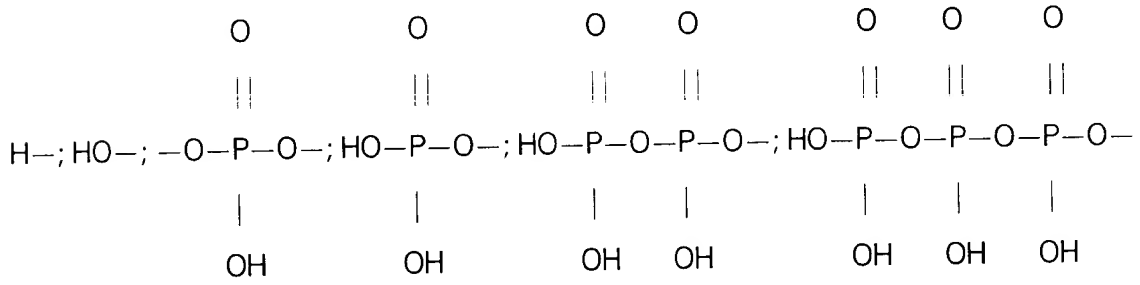
wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1' position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

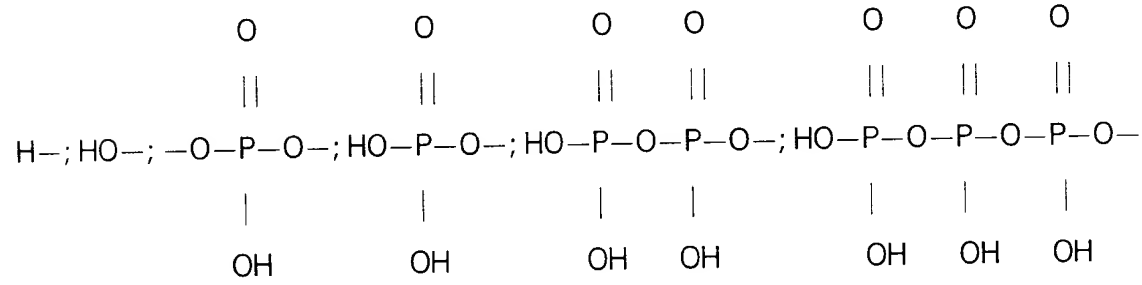
wherein B and A are covalently attached directly or through a linkage group, wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is

attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H– and HO– .

602. (Amended) The process according to claim 601, wherein y and z are H– .

603. (NEW) The process according to claim 569, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate.

604. (NEW) The process according to claim 600, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate.

605. (NEW) The process according to claims 569 or 600, wherein said sugar moiety or sugar analog comprises a monosaccharide.

606. (NEW) The process according to claim 605, wherein said monosaccharide comprises a furanose.

607. (NEW) The process according to claim 606, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose.

608. (NEW) The process according to claim 600, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

609. (NEW) The process according to claim 600, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

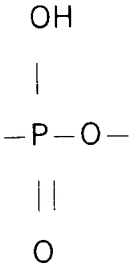
610. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof.

611. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N^4 position when said pyrimidine comprises cytosine, the N^2 position when said purine comprises adenine or deazaadenine, the N^6 position when said purine comprises guanine or deazaguanine, and combinations thereof.

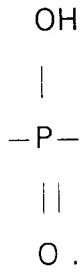
612. (NEW) The process according to claim 606, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

613. (NEW) The process according to claim 606, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

614 (NEW) The process according to claim 600, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



615. (NEW) The process according to claim 600, wherein PM is a mono-, di- or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen.

616. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

617. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

618. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group.

619. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

620. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety.

621. (NEW) The process according to claim 600, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

622. (NEW) The process according to claim 621, wherein said linkage group contains an amine.

623. (NEW) The process according to claim 622, wherein said amine comprises a primary amine.

624. (Amended) The process according to claim 621, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

625. (NEW) The process according to claim 601, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal.

626. (NEW) The process according to claim 601, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

627. (NEW) The process according to claim 601, wherein said covalent attachment comprises an allylamine group.

628. (NEW) The process according to claim 601, wherein said covalent attachment comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

629. (NEW) The process according to claim 601, wherein said covalent attachment includes a glycosidic linkage moiety.

630. (NEW) The process according to claim 601, wherein said A is covalently attached to B through a linkage group.

631. (NEW) The process according to claim 630, wherein said linkage group contains an amine.

632. (NEW) The process according to claim 631, wherein said amine comprises a primary amine.

633. (NEW) The process according to claim 630, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

634. (NEW) The process according to claim 600, wherein Sig comprises at least three carbon atoms.

635. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

636. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

637. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms.

638. (NEW) The process according to claim 637, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

639. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

640. (NEW) The process according to claim 639, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

641. (NEW) The process according to claim 600, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

642. (Amended) The process according to claim 600, wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component or a chelating component.

643. (NEW) The process according to claim 642, wherein Sig comprises an electron dense component.

645. (NEW) The process according to claim 642, wherein Sig comprises a magnetic component.

646. (NEW) The process according to claim 645, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

648. (Amended) The process according to claim 600, wherein Sig comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

649. (NEW) The process according to claim 648, wherein the binding protein comprises a lectin.

650. (NEW) The process according to claim 649, wherein the lectin comprises concanavalin A.

651. (NEW) The process according to claim 649, wherein said lectin is conjugated to ferritin.

654. (NEW) The process according to claim 642, wherein Sig comprises a hormone.

655. (NEW) The process according to claim 642, wherein Sig comprises a metal-containing component.

656. (NEW) The process according to claim 655, wherein said metal-containing component is catalytic.

657. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule.

658. (NEW) The process according to claim 657, wherein said indicator molecule comprises an aromatic compound.

659. (NEW) The process according to claim 658, wherein said aromatic compound is heterocyclic.

660. (NEW) The process according to claim 659, wherein said heterocyclic aromatic compound is fluorescent.

661. (NEW) The process according to claim 660, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing.

662. (NEW) The process according to claim 661, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

663. (NEW) The process according to claim 642, wherein Sig comprises a fluorescent component.

664. (NEW) The process according to claim 663, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

665. (NEW) The process according to claim 664, wherein said fluorescent component comprises fluorescein.

666. (NEW) The process according to claim 642, wherein Sig comprises a chemiluminescent component.

667. (NEW) The process according to claim 642, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

668. (NEW) The process according to claim 642, wherein Sig comprises an antibody component.

669. (NEW) The process according to claim 642, wherein Sig comprises a chelating component.

670. (Amended) The process according to claim 657, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing.

671. (NEW) The process according to claim 601, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

672. (NEW) The process according to claim 601, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms.

673. (NEW) The process according to claim 601, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

674. (NEW) The process according to claim 673, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

675. (NEW) The process according to claim 601, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

676. (NEW) The process according to claim 675, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

677. (NEW) The process according to claim 601, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide.

678. (Amended) The process according to claim 601, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

679. (NEW) The process according to claim 678, wherein A comprises an electron dense component.

681. (NEW) The process according to claim 680, wherein A comprises a magnetic component.

682. (NEW) The process according to claim 681, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

684. (Amended) The process according to claim 601, wherein A comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

685. (NEW) The process according to claim 684, wherein the binding protein comprises a lectin.

686. (NEW) The process according to claim 685, wherein the lectin comprises concanavalin A.

687. (NEW) The process according to claim 685, wherein said lectin is conjugated to ferritin.

690. (NEW) The process according to claim 678, wherein A comprises a hormone.

691. (NEW) The process according to claim 678, wherein A comprises a metal-containing component.

692. (NEW) The process according to claim 691, wherein said metal-containing component is catalytic.

693. (NEW) The process according to claim 601, wherein said A comprises an indicator molecule.

694. (NEW) The process according to claim 693, wherein said indicator molecule comprises an aromatic compound.

695. (NEW) The process according to claim 694, wherein said aromatic compound is heterocyclic.

696. (NEW) The process according to claim 695, wherein said heterocyclic aromatic compound is fluorescent.

697. (NEW) The process according to claim 696, wherein said fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing.

698. (NEW) The process according to claims 696 or 697, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

699. (NEW) The process according to claim 678, wherein A comprises a fluorescent component.

700. (NEW) The process according to claim 699, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

701. (NEW) The process according to claim 700, wherein said fluorescent component comprises fluorescein.

702. (NEW) The process according to claim 678, wherein A comprises a chemiluminescent component.

703. (NEW) The process according to claim 678, wherein A comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

704. (NEW) The process according to claim 678, wherein A comprises an antibody component.

705. (NEW) The process according to claim 678, wherein A comprises a chelating component.

706. (Amended) The process according to claim 693, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing.

707. (NEW) The process according to claim 569, wherein said labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of a fluorescent measurement, a chemiluminescent measurement, and a combination thereof.

708. (NEW) The process according to claim 569, wherein said subjecting step is carried out electrophoretically.

709. (NEW) The process according to claims 569, 600 or 601, wherein said detecting step is carried out directly.

710. (NEW) The process according to claim 709, wherein said direct detection is carried out using one or more indicator molecules.

711. (Amended) The process according to claim 710, wherein said one or more indicator molecules comprise fluorescent nucleotides or nucleotide analogs.

712. (Amended) The process according to claim 711, wherein said fluorescent nucleotides or nucleotide analogs comprise fluorescent DNA.

713. (Amended) The process according to claim 709, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more non-radioactively modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

714. (Amended) The process according to claim 713, wherein in said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound.

716. (Twice Amended) The process according to claims 569, 600 or 601, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said one or more non-radioactively modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

717. (NEW) The process according to claim 716, wherein in said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme.

719. (Twice Amended) The process according to claim 569, wherein said detectable non-radioactively modified or labeled nucleotides or nucleotide analogs are capable of being detected non-radioactively by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

720. (Amended) The process according to claim 569, wherein said detecting step comprises localizing said non-radioactively labeled nucleic acid fragments by means of said detectable non-radioactively modified or labeled nucleotides or nucleotide analogs.

721. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable non-radioactively labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactively modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more detectable non-radioactively modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

introducing or subjecting said detectable non-radioactively labeled fragments to a sequencing gel;

separating or resolving said fragments in said sequencing gel; and detecting non-radioactively each of the separated or resolved fragments; and determining the sequence of said nucleic acid of interest.

722. (NEW) The process according to claim 721, wherein the nucleic acid sequence of interest is derived from an organism.

723. (Amended) The process according to claims 722 or 726, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing.

724. (NEW) The process according to claim 723, wherein said organism comprises a mammal.

725. (NEW) The process according to claim 724, wherein said mammal comprises a human being.

726. (NEW) The process according to claim 721, wherein said organism is living.

727. (NEW) The process according to claims 722 or 726, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes.

728. (NEW) The process according to claim 727, wherein said organism comprises a eukaryote.

729. (NEW) The process according to claim 728, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome.

730. (NEW) The process according to claim 728, wherein said eukaryote comprises a mammal.

731. (NEW) The process according to claim 730, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome.

732. (NEW) The process according to claim 730, wherein said mammal comprises a human being.

733. (NEW) The process according to claim 732, wherein said human nucleic acid sequence of interest is contained within a chromosome.

734. (NEW) The process according to claim 733, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library.

735. (Amended) The process according to claim 721, wherein in said providing or generating step the fragments are provided or generated by one or more primers, nucleoside triphosphates or analogs thereof, or a combination thereof.

736. (NEW) The process according to claim 735, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing.

737. (NEW) The process according to claim 721, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

738. (Twice Amended) The process according to claim 721, wherein the detectable non-radioactively labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

739. (Amended) The process according to claim 721, wherein said providing or generating step, the one or more non-radioactively modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments.

740. (Amended) The process according to claim 739, wherein at least one of said non-radioactively modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments.

741. (NEW) The process according to claim 740, wherein said terminus comprises the 5' or the 3' terminus.

742. (NEW) The process according to claim 739, wherein said incorporation has been carried out in the presence of a primer.

743. (NEW) The process according to claim 721, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme.

744. (NEW) The process according to claim 743, wherein said enzyme comprises terminal transferase.

745. (NEW) The process according to claim 721, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling.

746. (Wholly Rewritten) The process according to claim 745, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

747. (NEW) The process according to claim 745, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase.

749. (NEW) The process according to claim 721 or 748, wherein said incorporation is carried out by means of a polymerizing enzyme.

750. (NEW) The process according to claim 749, wherein said polymerizing enzyme comprises a polymerase.

751. (NEW) The process according to claim 750, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase.

752. (Amended) The process according to claim 721, wherein said providing or generating step, the non-radioactively modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

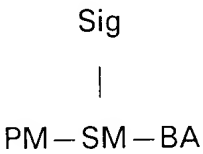
BASE is a pyrimidine, a purine or a 7-deazapurine base moiety

or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

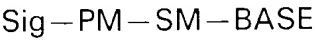
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

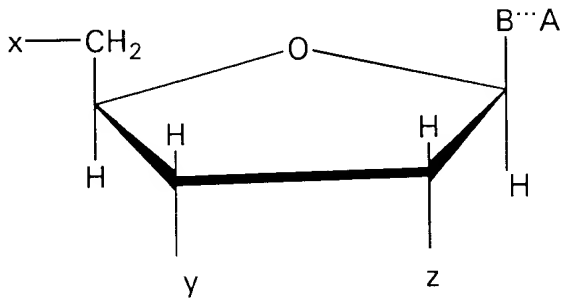
BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

753. (Amended) The process according to claim 721, wherein in said providing or generating step, the non-radioactively modified or labeled nucleotides or nucleotide analogs have the structure:

(i)



wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1'-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or

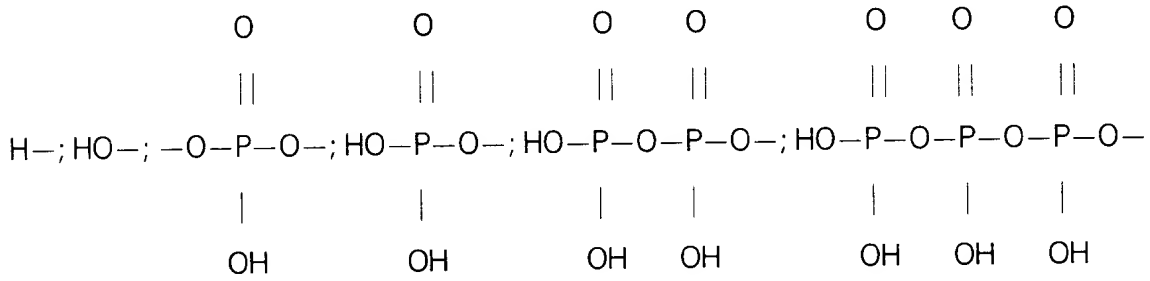
sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

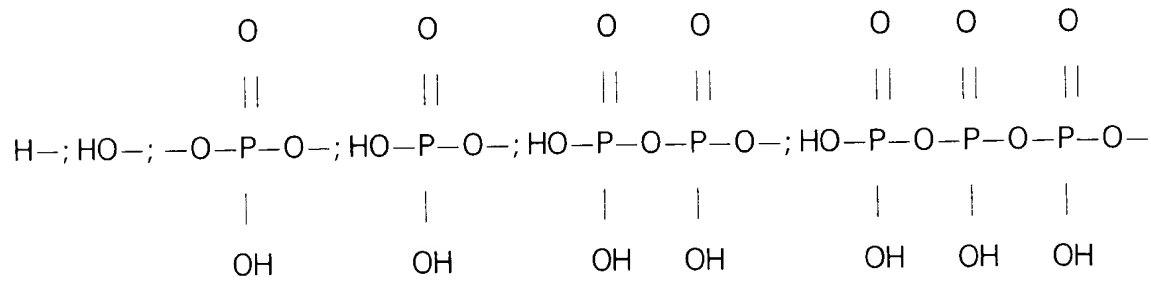
wherein B and A are covalently attached directly or through a linkage group,

wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H– and HO– .

754. (Amended) The process according to claim 753, wherein y and z are H– .

755. (NEW) The process according to claim 721, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate.

756. (NEW) The process according to claim 752, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate.

757. (NEW) The process according to claims 721 or 752, wherein said sugar moiety or sugar analog comprises a monosaccharide.

758. (NEW) The process according to claim 757, wherein said monosaccharide comprises a furanose.

759. (NEW) The process according to claim 758, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose.

760. (NEW) The process according to claim 752, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

761. (NEW) The process according to claim 752, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

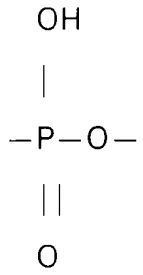
762. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof.

763. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N^4 position when said pyrimidine comprises cytosine, the N^2 position when said purine comprises adenine or deazaadenine, the N^6 position when said purine comprises guanine or deazaguanine, and combinations thereof.

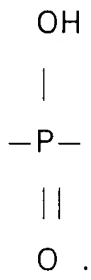
764. (NEW) The process according to claim 758, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

765. (NEW) The process according to claim 758, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

766. (NEW) The process according to claim 752, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



767. (NEW) The process according to claim 752, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen.

768. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

769. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

770. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group.

771. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

772. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety.

773. (NEW) The process according to claim 752, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

774. (NEW) The process according to claim 773, wherein said linkage group contains an amine.

775. (NEW) The process according to claim 774, wherein said amine comprises a primary amine.

776. (Amended) The process according to claim 773, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

777. (NEW) The process according to claim 753, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal.

778. (NEW) The process according to claim 753, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

779. (NEW) The process according to claim 753, wherein said covalent attachment comprises an allylamine group.

780. (NEW) The process according to claim 753, wherein said covalent attachment comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O- CH_2- \underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

781. (NEW) The process according to claim 753, wherein said covalent attachment includes a glycosidic linkage moiety.

782. (NEW) The process according to claim 753, wherein said A is covalently attached to B through a linkage group.

783. (NEW) The process according to claim 782, wherein said linkage group contains an amine.

784. (NEW) The process according to claim 783, wherein said amine comprises a primary amine.

785. (NEW) The process according to claim 782, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

786. (NEW) The process according to claim 752, wherein Sig comprises at least three carbon atoms.

787. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

788. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

789. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms.

790. (NEW) The process according to claim 789, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

791. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

792. (NEW) The process according to claim 791, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

793. (NEW) The process according to claim 752, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

794. (Amended) The process according to claim 752, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

795. (NEW) The process according to claim 794, wherein Sig comprises an electron dense component.

796. (NEW) The process according to claim 795, wherein said electron dense component comprises ferritin.

797. (NEW) The process according to claim 794, wherein Sig comprises a magnetic component.

800. (Amended) The process according to claim 752, wherein Sig comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

801. (NEW) The process according to claim 800, wherein the binding protein comprises a lectin.

802. (NEW) The process according to claim 801, wherein the lectin comprises concanavalin A.

803. (NEW) The process according to claim 801, wherein said lectin is conjugated to ferritin.

806. (NEW) The process according to claim 794, wherein Sig comprises a hormone.

807. (NEW) The process according to claim 794, wherein Sig comprises a metal-containing component.

808. (NEW) The process according to claim 807, wherein said metal-containing component is catalytic.

809. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule.

810. (NEW) The process according to claim 809, wherein said indicator molecule comprises an aromatic compound.

811. (NEW) The process according to claim 810, wherein said aromatic compound is heterocyclic.

812. (NEW) The process according to claim 811, wherein said heterocyclic aromatic compound is fluorescent.

813. (NEW) The process according to claim 812, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing.

814. (NEW) The process according to claim 813, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

815. (NEW) The process according to claim 794, wherein Sig comprises a fluorescent component.

816. (NEW) The process according to claim 815, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

817. (NEW) The process according to claim 816, wherein said fluorescent component comprises fluorescein.

818. (NEW) The process according to claim 794, wherein Sig comprises a chemiluminescent component.

819. (NEW) The process according to claim 794, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

820. (NEW) The process according to claim 794, wherein Sig comprises an antibody component.

821. (NEW) The process according to claim 794, wherein Sig comprises a chelating component.

822. (Amended) The process according to claim 809, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing.

823. (NEW) The process according to claim 753, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

824. (NEW) The process according to claim 753, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms.

825. (NEW) The process according to claim 753, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

826. (NEW) The process according to claim 825, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

827. (NEW) The process according to claim 753, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

828. (NEW) The process according to claim 827, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

829. (NEW) The process according to claim 753, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide.

830. (Amended) The process according to claim 753, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

831. (NEW) The process according to claim 830, wherein A comprises an electron dense component.

833. (NEW) The process according to claim 830, wherein A comprises a magnetic component.

834. (NEW) The process according to claim 833, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

836. (Amended) The process according to claim 753, wherein A comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

837. (NEW) The process according to claim 836, wherein the binding protein comprises a lectin.

838. (NEW) The process according to claim 837, wherein the lectin comprises concanavalin A.

839. (NEW) The process according to claim 837, wherein said lectin is conjugated to ferritin.

842. (NEW) The process according to claim 830, wherein A comprises a hormone.

843. (NEW) The process according to claim 830, wherein A comprises a metal-containing component.

844. (NEW) The process according to claim 843, wherein said metal-containing component is catalytic.

845. (NEW) The process according to claim 753, wherein said A comprises an indicator molecule.

846. (NEW) The process according to claim 845, wherein said indicator molecule comprises an aromatic compound.

847. (NEW) The process according to claim 846, wherein said aromatic compound is heterocyclic.

848. (NEW) The process according to claim 847, wherein said heterocyclic aromatic compound is fluorescent.

849. (NEW) The process according to claim 848, wherein said fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing.

850. (NEW) The process according to claims 848 or 849, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

851. (NEW) The process according to claim 830, wherein A comprises a fluorescent component.

852. (NEW) The process according to claim 851, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

853. (NEW) The process according to claim 852, wherein said fluorescent component comprises fluorescein.

854. (NEW) The process according to claim 830, wherein A comprises a chemiluminescent component.

855. (NEW) The process according to claim 830, wherein A comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

856. (NEW) The process according to claim 830, wherein A comprises an antibody component.

857. (NEW) The process according to claim 830, wherein A comprises a chelating component.

858. (Amended) The process according to claim 845, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing.

859. (Twice Amended) The process according to claim 721, wherein said detectable non-radioactively labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of a fluorescent measurement, a chemiluminescent measurement, and a combination thereof.

860. (NEW) The process according to claim 721, wherein said separating or resolving step is carried out electrophoretically.

861. (NEW) The process according to claims 721, 752 or 753, wherein said detecting step is carried out directly.

862. (NEW) The process according to claim 861, wherein said direct detection is carried out using one or more indicator molecules.

863. (Amended) The process according to claim 862, wherein said one or more indicator molecules comprise fluorescent nucleotides or nucleotide analogs.

864. (Amended) The process according to claim 863, wherein said fluorescent nucleotides or nucleotide analogs comprise fluorescent DNA.

865. (NEW) The process according to claim 861, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

866. (Amended) The process according to claim 865, wherein in said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound.

868. (Amended) The process according to claims 721, 752 or 753, wherein said detecting step is carried out by means of a indirectly detectable signal provided by said one or more non-radioactively modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

869. (NEW) The process according to claim 868, wherein in said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme.

871. (Twice Amended) The process according to claim 721, wherein said one or more modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

872. (Twice Amended) The process according to claim 721, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs.

873. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof;

detecting non-radioactively the detectable non-radioactive labeled nucleic acid fragments with a sequencing gel; and

determining the sequence of said nucleic acid of interest.

874. (NEW) The process according to claim 873, wherein the nucleic acid sequence of interest is derived from an organism.

875. (NEW) The process according to claim 874, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing.

876. (Amended) The process according to claims 875 or 878, wherein said organism comprises a mammal.

877. (NEW) The process according to claim 876, wherein said mammal comprises a human being.

878. (NEW) The process according to claim 874, wherein said organism is living.

879. (NEW) The process according to claims 874 or 878, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes.

880. (NEW) The process according to claim 879, wherein said organism comprises a eukaryote.

881. (NEW) The process according to claim 880, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome.

882. (NEW) The process according to claim 880, wherein said eukaryote comprises a mammal.

883. (NEW) The process according to claim 882, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome.

884. (NEW) The process according to claim 882, wherein said mammal comprises a human being.

885. (NEW) The process according to claim 884, wherein said human nucleic acid sequence of interest is contained within a chromosome.

886. (NEW) The process according to claim 885, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library.

887. (Amended) The process according to claim 873, wherein in said providing or generating step the fragments are provided or generated by one or more primers, nucleoside triphosphates or analogs thereof, or a combination thereof.

888. (NEW) The process according to claim 887, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing.

889. (NEW) The process according to claim 873, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

890. (Twice Amended) The process according to claim 873, wherein the detectable non-radioactive labeled complementary nucleic acid is fragmented and separated prior to detecting in said sequencing gel.

891. (Amended) The process according to claim 873, wherein in said providing or generating step, the one or more non-radioactive modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments.

892. (Amended) The process according to claim 891, wherein at least one of said non-radioactive modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments.

893. (NEW) The process according to claim 892, wherein said terminus comprises the 5' or the 3' terminus.

894. (NEW) The process according to claim 891, wherein said incorporation has been carried out in the presence of a primer.

895. (NEW) The process according to claim 873, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme.

896. (NEW) The process according to claim 895, wherein said enzyme comprises terminal transferase.

897. (NEW) The process according to claim 873, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling.

898. (Wholly Rewritten) The process according to claim 897, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

899. (NEW) The process according to claim 898, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase.

901. (NEW) The process according to claim 873 or 900, wherein said incorporation is carried out by means of a polymerizing enzyme.

902. (NEW) The process according to claim 901, wherein said polymerizing enzyme comprises a polymerase.

903. (NEW) The process according to claim 902, wherein said polymerizing enzyme is selected from the group consisting of DNA polymerase and RNA polymerase.

904. (Amended) The process according to claim 873, wherein in said providing or generating step, the non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

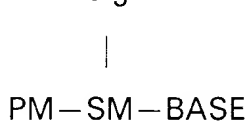
BASE is a pyrimidine, a purine or a 7-deazapurine base moiety

or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

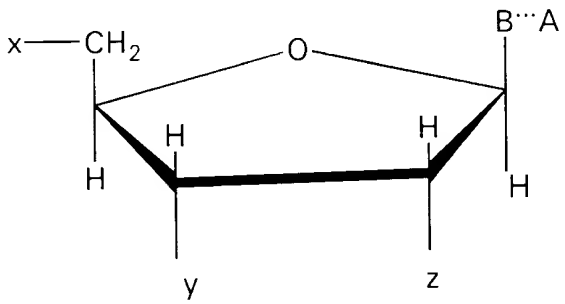
BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

905. (Amended) The process according to claim 873, wherein in said providing or generating step, the non-radioactive modified or labeled nucleotides or nucleotide analogs have the structure:

(i)



wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety or an analog of any of the foregoing, and B is covalently bonded to the C1'-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or

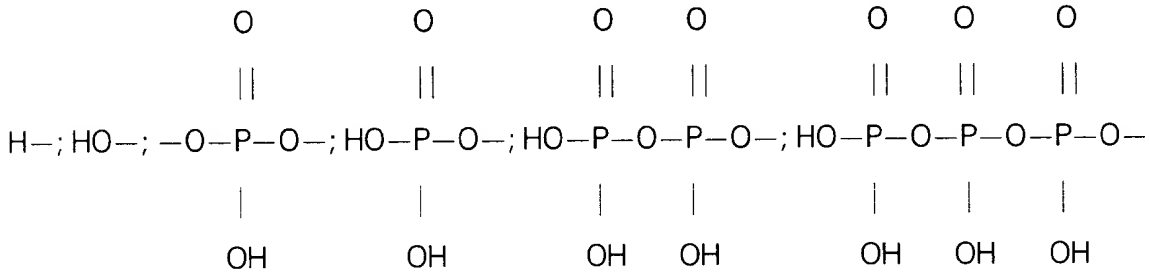
sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

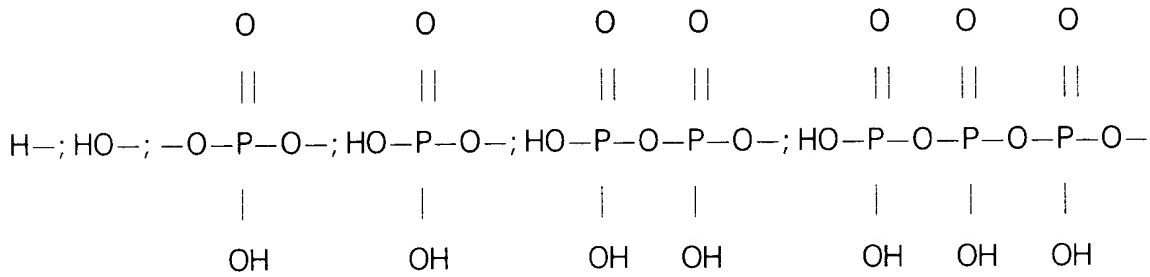
wherein B and A are covalently attached directly or through a linkage group,

wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H- and HO-.

906. (Amended) The process according to claim 905, wherein y and z are H—.

907. (NEW) The process according to claim 873, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate.

908. (NEW) The process according to claim 904, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate.

909. (NEW) The process according to claims 873 or 904, wherein said sugar moiety or sugar analog comprises a monosaccharide.

910. (NEW) The process according to claim 909, wherein said monosaccharide comprises a furanose.

911. (NEW) The process according to claim 910, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose.

912. (NEW) The process according to claim 904, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

913. (NEW) The process according to claim 904, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

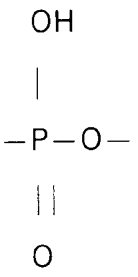
914. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof.

915. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N^4 position when said pyrimidine comprises cytosine, the N^2 position when said purine comprises adenine or deazaadenine, the N^6 position when said purine comprises guanine or deazaguanine, and combinations thereof.

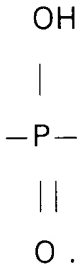
916. (NEW) The process according to claim 910, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

917. (NEW) The process according to claim 910, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

918. (NEW) The process according to claim 904, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



919. (NEW) The process according to claim 904, wherein PM is a mono-, di- or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen.

920. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

921. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

922. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group.

923. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

924. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety.

925. (NEW) The process according to claim 904, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

926. (NEW) The process according to claim 925, wherein said linkage group contains an amine.

927. (NEW) The process according to claim 926, wherein said amine comprises a primary amine.

928. (Amended) The process according to claim 925, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

929. (NEW) The process according to claim 905, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal.

930. (NEW) The process according to claim 905, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

931. (NEW) The process according to claim 905, wherein said covalent attachment comprises an allylamine group.

932. (NEW) The process according to claim 905, wherein said covalent attachment comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O- CH_2- \underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

933. (NEW) The process according to claim 905, wherein said covalent attachment includes a glycosidic linkage moiety.

934. (NEW) The process according to claim 905, wherein said A is covalently attached to B through a linkage group.

935. (NEW) The process according to claim 934, wherein said linkage group contains an amine.

936. (NEW) The process according to claim 935, wherein said amine comprises a primary amine.

937. (NEW) The process according to claim 934, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

938. (NEW) The process according to claim 904, wherein Sig comprises at least three carbon atoms.

939. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

940. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

941. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms.

942. (NEW) The process according to claim 941, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

943. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

944. (NEW) The process according to claim 943, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

945. (NEW) The process according to claim 904, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

946. (Amended) The process according to claim 904, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

947. (NEW) The process according to claim 946, wherein Sig comprises an electron dense component.

949. (NEW) The process according to claim 946, wherein Sig comprises a magnetic component.

950. (NEW) The process according to claim 949, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

952. (Amended) The process according to claim 904, wherein Sig comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

953. (NEW) The process according to claim 952, wherein the binding protein comprises a lectin.

954. (NEW) The process according to claim 953, wherein the lectin comprises concanavalin A.

955. (NEW) The process according to claim 953, wherein said lectin is conjugated to ferritin.

958. (NEW) The process according to claim 946, wherein Sig comprises a hormone.

959. (NEW) The process according to claim 946, wherein Sig comprises a metal-containing component.

960. (NEW) The process according to claim 959, wherein said metal-containing component is catalytic.

961. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule.

962. (NEW) The process according to claim 961, wherein said indicator molecule comprises an aromatic compound.

963. (NEW) The process according to claim 962, wherein said aromatic compound is heterocyclic.

964. (NEW) The process according to claim 963, wherein said heterocyclic aromatic compound is fluorescent.

965. (NEW) The process according to claim 904, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing.

966. (NEW) The process according to claim 965, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

967. (NEW) The process according to claim 946, wherein Sig comprises a fluorescent component.

968. (NEW) The process according to claim 967, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

969. (NEW) The process according to claim 968, wherein said fluorescent component comprises fluorescein.

970. (NEW) The process according to claim 946, wherein Sig comprises a chemiluminescent component.

971. (NEW) The process according to claim 946, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

972. (NEW) The process according to claim 946, wherein Sig comprises an antibody component.

973. (NEW) The process according to claim 946, wherein Sig comprises a chelating component.

974. (Amended) The process according to claim 961, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing.

975. (NEW) The process according to claim 905, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

976. (NEW) The process according to claim 905, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms.

977. (NEW) The process according to claim 905, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

978. (NEW) The process according to claim 977, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

979. (NEW) The process according to claim 905, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

980. (NEW) The process according to claim 979, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

981. (NEW) The process according to claim 905, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide.

982. (Amended) The process according to claim 905, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

983. (NEW) The process according to claim 982, wherein A comprises an electron dense component.

985. (NEW) The process according to claim 982, wherein A comprises a magnetic component.

986. (NEW) The process according to claim 985, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

988. (Amended) The process according to claim 905, wherein A comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

989. (NEW) The process according to claim 988, wherein the binding protein comprises a lectin.

990. (NEW) The process according to claim 989, wherein the lectin comprises concanavalin A.

991. (NEW) The process according to claim 989, wherein said lectin is conjugated to ferritin.

994. (NEW) The process according to claim 982, wherein A comprises a hormone.

995. (NEW) The process according to claim 982, wherein A comprises a metal-containing component.

996. (NEW) The process according to claim 995, wherein said metal-containing component is catalytic.

997. (NEW) The process according to claim 905, wherein said A comprises an indicator molecule.

998. (NEW) The process according to claim 997, wherein said indicator molecule comprises an aromatic compound.

999. (NEW) The process according to claim 998, wherein said aromatic compound is heterocyclic.

1000. (NEW) The process according to claim 999, wherein said heterocyclic aromatic compound is fluorescent.

1001. (NEW) The process according to claim 1000, wherein said fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing.

1002. (NEW) The process according to claims 1000 or 1001, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

1003. (NEW) The process according to claim 982, wherein A comprises a fluorescent component.

1004. (NEW) The process according to claim 1003, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

1005. (NEW) The process according to claim 1004, wherein said fluorescent component comprises fluorescein.

1006. (NEW) The process according to claim 982, wherein A comprises a chemiluminescent component.

1007. (NEW) The process according to claim 982, wherein A comprises an antigenic or hapten component capable of completing with an antibody specific to the component.

1008. (NEW) The process according to claim 982, wherein A comprises an antibody component.

1009. (NEW) The process according to claim 982, wherein A comprises a chelating component.

1010. (Amended) The process according to claim 1009, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing.

1011. (Twice Amended) The process according to claim 873, wherein said detectable non-radioactive labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of a fluorescent measurement, a chemiluminescent measurement, and a combination thereof.

1012. (Twice Amended) The process according to claim 873, wherein said detecting step, the detectable non-radioactive labeled nucleic acid fragments are separated or resolved electrophoretically.

1013. (NEW) The process according to claims 873, 904 or 905, wherein said detecting step is carried out directly.

1014. (NEW) The process according to claim 1013, wherein said direct detection is carried out using one or more indicator molecules.

1015. (Amended) The process according to claim 1014, wherein said one or more indicator molecules comprise fluorescent nucleotides or nucleotide analogs.

1016. (Amended) The process according to claim 1015, wherein said fluorescent nucleotides or nucleotide analogs comprise fluorescent DNA.

1017. (Amended) The process according to claim 1016, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

1018. (Amended) The process according to claim 1013, wherein said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound.

1020. (Amended) The process according to claims 873, 904 or 905, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

1021. (NEW) The process according to claim 1020, wherein said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme.

1023. (Twice Amended) The process according to claim 873, wherein said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1024. (Twice Amended) The process according to claim 873, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs.

1025. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the step of detecting non-radioactively with a sequencing gel one or more detectable non-radioactive labeled nucleic acid fragments comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs have been modified on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the base moiety or the base analog thereof.

1026. (NEW) The process according to claim 1025, wherein the nucleic acid sequence of interest is derived from an organism.

1027. (Amended) The process according to claims 1026 or 1030, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing.

1028. (NEW) The process according to claim 1027, wherein said organism comprises a mammal.

1029. (NEW) The process according to claim 1028, wherein said mammal comprises a human being.

1030. (NEW) The process according to claim 1026, wherein said organism is living.

1031. (NEW) The process according to claims 1026 or 1030, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes.

1032. (NEW) The process according to claim 1031, wherein said organism comprises a eukaryote.

1033. (NEW) The process according to claim 1032, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome.

1034. (NEW) The process according to claim 1032, wherein said eukaryote comprises a mammal.

1035. (NEW) The process according to claim 1034, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome.

1036. (NEW) The process according to claim 1034, wherein said mammal comprises a human being.

1037. (NEW) The process according to claim 1036, wherein said human nucleic acid sequence of interest is contained within a chromosome.

1038. (NEW) The process according to claim 1037, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library.

1039. (Amended) The process according to claim 1025, wherein prior to said detecting step the fragments are provided or generated by one or more primers, nucleoside triphosphates or analogs thereof, or a combination thereof.

1040. (NEW) The process according to claim 1039, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing.

1041. (NEW) The process according to claim 1025, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

1042. (Twice Amended) The process according to claim 1025, wherein the detectable non-radioactive labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

1043. (Twice Amended) The process according to claim 1025, wherein prior to said detecting step, the one or more non-radioactive modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments.

1044. (Amended) The process according to claim 1043, wherein at least one of said non-radioactive modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments.

1045. (NEW) The process according to claim 1044, wherein said terminus comprises the 5' or the 3' terminus.

1046. (NEW) The process according to claim 1043, wherein said incorporation has been carried out in the presence of a primer.

1047. (NEW) The process according to claim 1025, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme.

1048. (NEW) The process according to claim 1047, wherein said enzyme comprises terminal transferase.

1049. (NEW) The process according to claim 1025, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling.

1050. (Wholly Rewritten) The process according to claim 1049, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

1051. (NEW) The process according to claim 1049, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase.

1053. (NEW) The process according to claim 1025 or 1052, wherein said incorporation is carried out by means of a polymerizing enzyme.

1054. (NEW) The process according to claim 1053, wherein said polymerizing enzyme comprises a polymerase.

1055. (NEW) The process according to claim 1054, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase.

1056. (Twice Amended) The process according to claim 1025, wherein in said detecting step, the non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

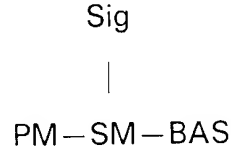
BASE is a pyrimidine, a purine or a 7-deazapurine base moiety

or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

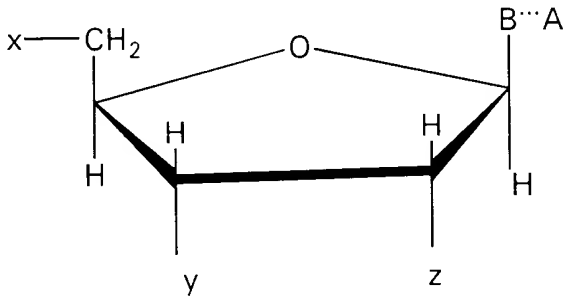
BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

1057. (Twice Amended) The process according to claim 1025, wherein prior to said detecting step, the non-radioactive modified or labeled nucleotides or nucleotide analogs have the structure:

(i)



wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1'-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof,

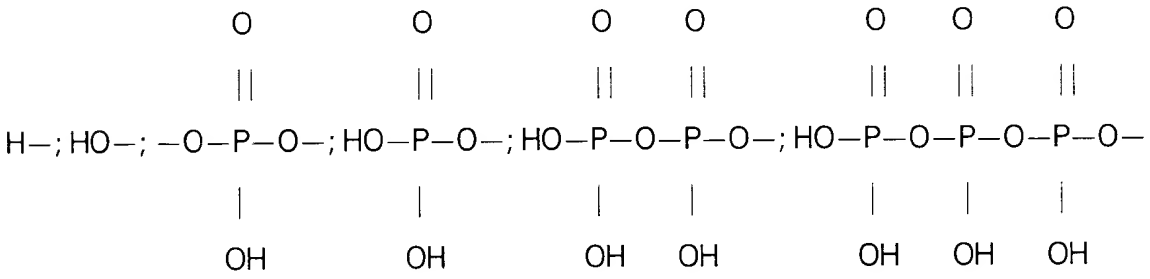
and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

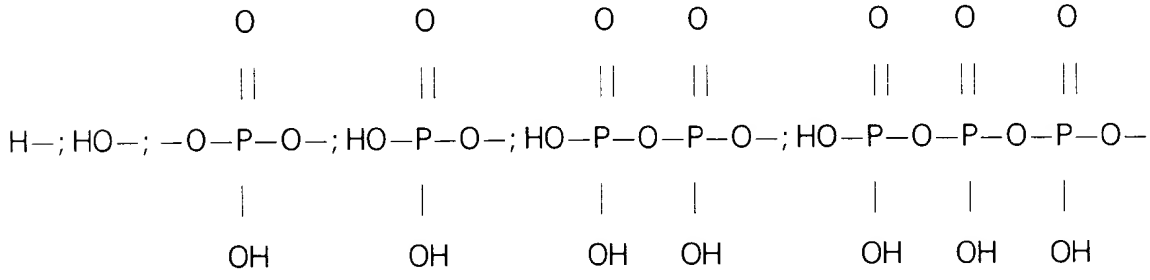
wherein B and A are covalently attached directly or through a linkage group,

wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H– and HO–.

1058. (Amended) The process according to claim 1057, wherein y and z are H—.

1059. (NEW) The process according to claim 1025, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate.

1060. (NEW) The process according to claim 1056, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate.

1061. (NEW) The process according to claims 1025 or 1056, wherein said sugar moiety or sugar analog comprises a monosaccharide.

1062. (NEW) The process according to claim 1061, wherein said monosaccharide comprises a furanose.

1063. (NEW) The process according to claim 1062, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose.

1064. (NEW) The process according to claim 1056, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

1065. (NEW) The process according to claim 1056, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

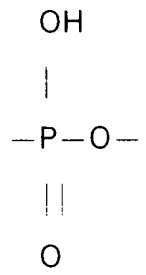
1066. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety in said nucleotide M is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof.

1067. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N^4 position when said pyrimidine comprises cytosine, the N^2 position when said purine comprises adenine or deazaadenine, the N^6 position when said purine comprises guanine or deazaguanine, and combinations thereof.

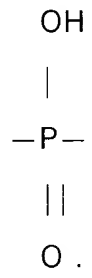
1068. (NEW) The process according to claim 1062, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

1069. (NEW) The process according to claim 1062, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

1070. (NEW) The process according to claim 1056, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



1071. (NEW) The process according to claim 1056, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen.

1072. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

1073. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

1074. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group.

1075. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

1076. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety.

1077. (NEW) The process according to claim 1056, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

1078. (NEW) The process according to claim 1077, wherein said linkage group contains an amine.

1079. (NEW) The process according to claim 1078, wherein said amine comprises a primary amine.

1080. (NEW) The process according to claim 1077, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

1081. (NEW) The process according to claim 1057, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal.

1082. (NEW) The process according to claim 1057, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

1083. (NEW) The process according to claim 1057, wherein said covalent attachment comprises an allylamine group.

1084. (NEW) The process according to claim 1057, wherein said covalent attachment comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O- CH_2- \underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

1085. (NEW) The process according to claim 1057, wherein said covalent attachment includes a glycosidic linkage moiety.

1086. (NEW) The process according to claim 1057, wherein said A is covalently attached to B through a linkage group.

1087. (NEW) The process according to claim 1086, wherein said linkage group contains an amine.

1088. (NEW) The process according to claim 1087, wherein said amine comprises a primary amine.

1089. (NEW) The process according to claim 1086, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

1090. (NEW) The process according to claim 1056, wherein Sig comprises at least three carbon atoms.

1091. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

1092. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

1093. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms.

1094. (NEW) The process according to claim 1093, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

1095. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

1096. (NEW) The process according to claim 1095, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

1097. (NEW) The process according to claim 1056, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

1098. (Amended) The process according to claim 1056, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

1099. (NEW) The process according to claim 1098, wherein Sig comprises an electron dense component.

1101. (NEW) The process according to claim 1098, wherein Sig comprises a magnetic component.

1102. (NEW) The process according to claim 1101, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

1104. (Amended) The process according to claim 1056, wherein Sig comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

1105. (NEW) The process according to claim 1104, wherein the binding protein comprises a lectin.

1106. (NEW) The process according to claim 1105, wherein the lectin comprises concanavalin A.

1107. (NEW) The process according to claim 1105, wherein said lectin is conjugated to ferritin.

1110. (NEW) The process according to claim 1098, wherein Sig comprises a hormone.

1111. (NEW) The process according to claim 1098, wherein Sig comprises a metal-containing component.

1112. (NEW) The process according to claim 1111, wherein said metal-containing component is catalytic.

1113. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule.

1114. (NEW) The process according to claim 1113, wherein said indicator molecule comprises an aromatic compound.

1115. (NEW) The process according to claim 1114, wherein said aromatic compound is heterocyclic.

1116. (NEW) The process according to claim 1115, wherein said heterocyclic aromatic compound is fluorescent.

1117. (NEW) The process according to claim 1116, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing.

1118. (NEW) The process according to claim 1117, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

1119. (NEW) The process according to claim 1098, wherein Sig comprises a fluorescent component.

1120. (NEW) The process according to claim 1119, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

1121. (NEW) The process according to claim 1120, wherein said fluorescent component comprises fluorescein.

1122. (NEW) The process according to claim 1098, wherein Sig comprises a chemiluminescent component.

1123. (NEW) The process according to claim 1098, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

1124. (NEW) The process according to claim 1098, wherein Sig comprises an antibody component.

1125. (NEW) The process according to claim 1098, wherein Sig comprises a chelating component.

1126. (Amended) The process according to claim 1113, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing.

1127. (NEW) The process according to claim 1057, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

1128. (NEW) The process according to claim 1057, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms.

1129. (NEW) The process according to claim 1057, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

1130. (NEW) The process according to claim 1129, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

1131. (NEW) The process according to claim 1057, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

1132. (NEW) The process according to claim 1131, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent.

1133. (NEW) The process according to claim 1057, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide.

1134. (Amended) The process according to claim 1057, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

1135. (NEW) The process according to claim 1134, wherein A comprises an electron dense component.

1137. (NEW) The process according to claim 1134, wherein A comprises a magnetic component.

1138. (NEW) The process according to claim 1137, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

1140. (Amended) The process according to claim 1057, wherein A comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

1141. (NEW) The process according to claim 1140, wherein the binding protein comprises a lectin.

1142. (NEW) The process according to claim 1141, wherein the lectin comprises concanavalin A.

1143. (NEW) The process according to claim 1141, wherein said lectin is conjugated to ferritin.

1146. (NEW) The process according to claim 1134, wherein A comprises a hormone.

1147. (NEW) The process according to claim 1134, wherein A comprises a metal-containing component.

1148. (NEW) The process according to claim 1147, wherein said metal-containing component is catalytic.

1149. (NEW) The process according to claim 1057, wherein said A comprises an indicator molecule.

1150. (NEW) The process according to claim 1149, wherein said indicator molecule comprises an aromatic compound.

1151. (NEW) The process according to claim 1150, wherein said aromatic compound is heterocyclic.

1152. (NEW) The process according to claim 1151, wherein said heterocyclic aromatic compound is fluorescent.

1153. (NEW) The process according to claim 1152, wherein said fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing.

1154. (NEW) The process according to claims 1152 or 1153, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

1155. (NEW) The process according to claim 1154, wherein A comprises a fluorescent component.

1156. (NEW) The process according to claim 1155, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

1157. (NEW) The process according to claim 1156, wherein said fluorescent component comprises fluorescein.

1158. (NEW) The process according to claim 1134, wherein A comprises a chemiluminescent component.

1159. (NEW) The process according to claim 1134, wherein A comprises an antigenic or hapten component capable of completing with an antibody specific to the component.

1160. (NEW) The process according to claim 1134, wherein A comprises an antibody component.

1161. (NEW) The process according to claim 1134, wherein A comprises a chelating component.

1162. (Amended) The process according to claim 1149, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing.

1163. (Twice Amended) The process according to claim 1025, wherein said detectable labeled nucleic acid fragments are detectable non-radioactively by a fluorescent measurement, a chromogenic measurement, a chemiluminescent measurement, or a combination thereof.

1164. (Twice Amended) The process according to claim 1025, wherein said detecting step, the detectable non-radioactive labeled nucleic acid fragments are separated or resolved electrophoretically.

1165. (NEW) The process according to claims 1025, 1056 or 1057, wherein said detecting step is carried out directly.

1166. (NEW) The process according to claim 1165, wherein said direct detection is carried out using one or more indicator molecules.

1167. (Amended) The process according to claim 1166, wherein said one or more indicator molecules comprise fluorescent nucleotides or nucleotide analogs.

1168. (Amended) The process according to claim 1167, wherein said fluorescent nucleotides or nucleotide analogs comprise fluorescent DNA.

1169. (Amended) The process according to claim 1165, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

1170. (Amended) The process according to claim 1165, wherein said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound.

1172. (Amended) The process according to claims 1025, 1056 or 1057, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

1173. (NEW) The process according to claim 1172, wherein said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme.

1175. (Twice Amended) The process according to claim 1025, wherein said one or more modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1176. (Twice Amended) The process according to claim 1025, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said one or more modified or labeled nucleotides or nucleotide analogs.

1177. (Twice Amended) A process for determining with a sequencing gel the presence of nucleic acid fragments comprising a sequence complementary to a nucleic acid of interest or a portion thereof, said process comprising the steps of:

(A) providing

(i) one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into a nucleic acid; or

(ii) one or more oligonucleotides or polynucleotides comprising at least one said detectable non-radioactive chemically modified or labeled nucleotide or nucleotide analog; or

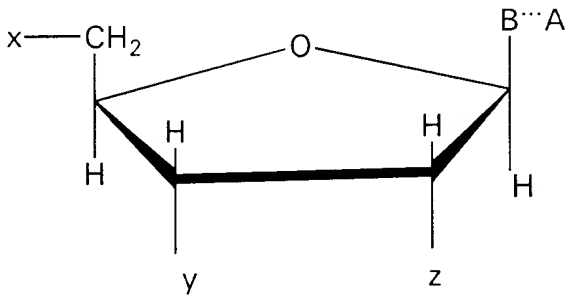
(iii) both (i) and (ii);

wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs (i) and said oligonucleotides and polynucleotides (ii) are capable of attaching to or coupling to or incorporating into or forming one or more nucleic acid fragments, and wherein said detectable non-radioactive chemically

modified or labeled nucleotides or nucleotide analogs have been modified or labeled non-disruptively or disruptively on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof; and;

(B) incorporating said one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs (i) or said one or more oligonucleotides or polynucleotides comprising at least one chemically modified or labeled nucleotides or nucleotide analogs (ii), or both (i) and (ii), into one or more nucleic acid fragments, to prepare detectable non-radioactive labeled fragments, each such fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof and said one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs, and wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i)



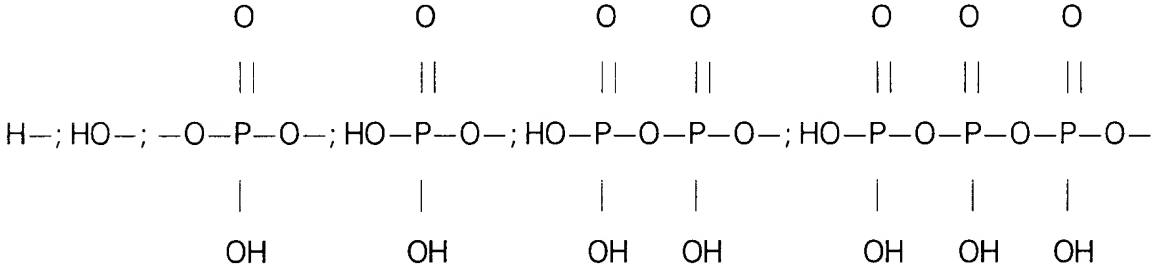
wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar

moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

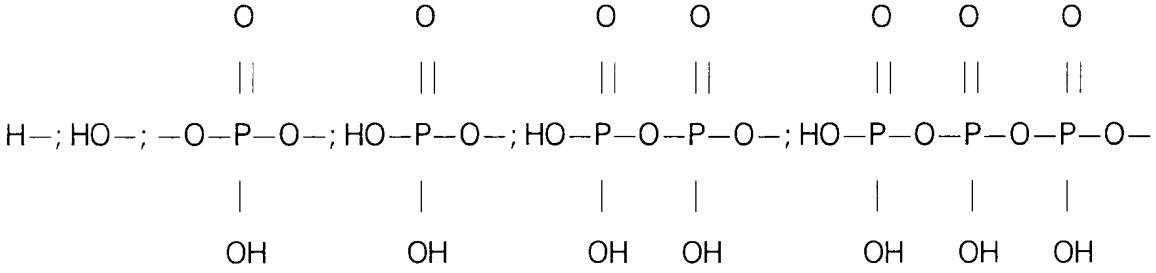
wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

wherein B and A are covalently attached directly or through a linkage group, and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H– and HO– ;

(ii)

wherein

PM is a phosphate moiety or phosphate analog,

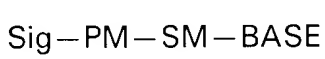
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety, and

wherein said PM is covalently attached to SM, said BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is detectable non-radioactive moiety; and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

(C) transferring or subjecting said detectable non-radioactive labeled fragments to a sequencing gel;

(D) separating or resolving said detectable non-radioactive labeled fragments; and

(E) non-radioactively detecting directly or indirectly the presence of said detectable non-radioactive labeled fragments to determine the sequence of said nucleic acid of interest.

1178. (NEW) The process according to claim 1177, wherein the nucleic acid sequence of interest is derived from an organism.

1179. (Amended) The process according to claims 1178 or 1182, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing.

1180. (NEW) The process according to claim 1179, wherein said organism comprises a mammal.

1181. (NEW) The process according to claim 1180, wherein said mammal comprises a human being.

1182. (NEW) The process according to claim 1178, wherein said organism is living.

1183. (NEW) The process according to claims 1178 or 1182, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes.

1184. (NEW) The process according to claim 1183, wherein said organism comprises a eukaryote.

1185. (NEW) The process according to claim 1184, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome.

1186. (NEW) The process according to claim 1184, wherein said eukaryote comprises a mammal.

1187. (NEW) The process according to claim 1186, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome.

1188. (NEW) The process according to claim 1186, wherein said mammal comprises a human being.

1189. (NEW) The process according to claim 1188, wherein said human nucleic acid sequence of interest is contained within a chromosome.

1190. (NEW) The process according to claim 1189, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library.

1191. (NEW) The process according to claim 1177, wherein said incorporating step is carried out using an enzyme.

1192. (NEW) The process according to claim 1191, wherein said enzyme comprises a polymerase.

1193. (NEW) The process according to claim 1192, wherein said polymerase comprises DNA polymerase.

1194. (NEW) The process according to claim 1177, wherein said one or more chemically modified nucleotides or said other modified or unmodified nucleic acids comprise a nucleoside di- or tri-phosphate.

1195. (NEW) The process according to claim 1177, wherein said incorporating step is template dependent or template independent.

1196. (NEW) The process according to claim 1177, wherein said incorporating step is template dependent.

1197. (Amended) The process according to claim 1177, wherein the detectable labeled nucleic acid fragments prepared by said incorporating step comprises at least one internal modified nucleotide.

1198. (Amended) The process according to claim 1177, wherein the detectable labeled nucleic acid fragments prepared by said incorporating step comprises at least one terminal modified nucleotide.

1199. (NEW) The process according to claim 1177, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme.

1200. (NEW) The process according to claim 1199, wherein said enzyme comprises terminal transferase.

1201. (NEW) The process according to claim 1177, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling.

1202. (Wholly Rewritten) The process according to claim 1201, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

1203. (NEW) The process according to claim 1201, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase.

1204. (NEW) The process according to claim 1177, wherein said incorporation comprises nick translation.

1205. (NEW) The process according to claim 1177 or 1204, wherein said incorporation is carried out by means of a polymerizing enzyme.

1206. (NEW) The process according to claim 1205, wherein said polymerizing enzyme comprises a polymerase.

1207. (NEW) The process according to claim 1206, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase.

1208. (NEW) The process according to claim 1177, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a monophosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate.

1209. (NEW) The process according to claim 1177, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate.

1210. (NEW) The process according to claim 1177, wherein said sugar moiety or sugar analog comprises a monosaccharide.

1211. (NEW) The process according to claim 1210, wherein said monosaccharide comprises a furanose.

1212. (NEW) The process according to claim 1211, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose.

1213. (NEW) The process according to claim 1177, wherein said B in nucleotide or nucleotide analog (i) or said BASE in nucleotides or nucleotide analogs (ii) or (iii) is selected from the group consisting of a pyrimidine moiety or pyrimidine analog, a purine moiety or purine analog, a 7-deazapurine moiety and a 7-deazapurine analog, and a combination of any of the foregoing.

1214. (NEW) The process according to claim 1177, wherein in said chemically modified nucleotides or nucleotide analogs (i) when B is a purine or a purine analog, A is attached to the 8-position of the purine moiety or the purine analog, when B is a 7-deazapurine moiety or a 7-deazapurine analog, A is attached to the 7-position of the deazapurine moiety or the 7-deazapurine analog, and when B is a pyrimidine moiety or a pyrimidine analog, A is attached to the 5-position of the pyrimidine moiety or the pyrimidine analog.

1215. (NEW) The process according to claim 1177, wherein in said chemically modified nucleotides or nucleotide analogs (i) A is covalently attached to said B at a position when B is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to B at a position when B is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof.

1216. (NEW) The process according to claim 1177, wherein in said chemically modified nucleotides or nucleotide analogs (i) A is covalently attached to said B at a position selected from the group consisting of the N^4 position when said pyrimidine comprises cytosine, the N^2 position when said purine comprises adenine or deazaadenine, the N^6 position when said purine comprises guanine or deazaguanine, and combinations thereof.

1217. (NEW) The process according to claim 1177, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i) or (iii) or both is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

1218. (NEW) The process according to claim 1177, wherein said incorporating step, A in the nucleotide (i) is covalently attached to B through a linkage group.

1219. (NEW) The process according to claim 1218, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

1220. (NEW) The process according to claim 1218, wherein said linkage group contains an amine.

1221. (NEW) The process according to claim 1220, wherein said amine comprises a primary amine.

1222. (NEW) The process according to claim 1177, wherein said incorporating step, Sig in the nucleotide (ii) is covalently attached to SM through a linkage group.

1223. (NEW) The process according to claim 1222, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

1224. (NEW) The process according to claim 1222, wherein said linkage group contains an amine.

1225. (NEW) The process according to claim 1224, wherein said amine comprises a primary amine.

1226. (NEW) The process according to claim 1177, wherein said incorporating step, Sig in the nucleotide (iii) is covalently attached to PM through a linkage group.

1227. (NEW) The process according to claim 1226, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

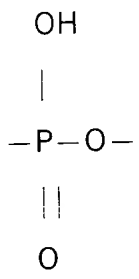
1228. (NEW) The process according to claim 1226, wherein said linkage group contains an amine.

1229. (NEW) The process according to claim 1228, wherein said amine comprises a primary amine.

1230. (NEW) The process according to claim 1211, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

1231. (NEW) The process according to claim 1211, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

1232. (NEW) The process according to claim 1177, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



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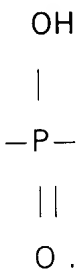


1233. (NEW) The process according to claim 1177, wherein PM is a mono-, di- or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen.

1234. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal.

1235. (Amended) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

1236. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group.

1237. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

1238. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety.

1239. (NEW) The process according to claim 1177, wherein in said nucleotides or nucleotide analogs (i), A is covalently attached to B through a linkage group, or in said nucleotides or nucleotide analogs (ii) or (iii), Sig is covalently attached to BASE, SM or PM through a linkage group.

1240. (NEW) The process according to claim 1239, wherein said linkage group contains an amine.

1241. (NEW) The process according to claim 1240, wherein said amine comprises a primary amine.

1242. (NEW) The process according to claim 1239, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

1243. (NEW) The process according to claim 1177, wherein said A or Sig comprises at least three carbon atoms.

1244. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

1245. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

1246. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

1247. (NEW) The process according to claim 1141, wherein said A or Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

1248. (NEW) The process according to claim 1177, wherein said A or Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

1249. (Amended) The process according to claim 1177, wherein said A or Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

1250. (NEW) The process according to claim 1249, wherein said A or Sig comprises an electron dense component.

1252. (NEW) The process according to claim 1249, wherein said A or Sig comprises a magnetic component.

1253. (NEW) The process according to claim 1252, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

1255. (Amended) The process according to claim 1177, wherein said A or Sig comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

1256. (NEW) The process according to claim 1255, wherein the binding protein comprises a lectin.

1257. (NEW) The process according to claim 1256, wherein the lectin comprises concanavalin A.

1258. (NEW) The process according to claim 1256, wherein said lectin is conjugated to ferritin.

1260. (NEW) The process according to claim 1259, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, ß-galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof.

1261. (NEW) The process according to claim 1249, wherein said A or Sig comprises a hormone.

1262. (NEW) The process according to claim 1249, wherein said A or Sig comprises a metal-containing component.

1263. (NEW) The process according to claim 1262, wherein said metal-containing component is catalytic.

1264. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an indicator molecule.

1265. (NEW) The process according to claim 1264, wherein said indicator molecule comprises an aromatic compound.

1266. (NEW) The process according to claim 1265, wherein said aromatic compound is heterocyclic.

1267. (NEW) The process according to claim 1266, wherein said heterocyclic aromatic compound is fluorescent.

1268. (NEW) The process according to claim 1267, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine and dansyl.

1269. (NEW) The process according to claim 1268, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

1270. (Amended) The process according to claim 1264, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, and a chelating component, and a combination of any of the foregoing.

1271. (NEW) The process according to claim 1249, wherein said A or Sig comprises a fluorescent component.

1272. (NEW) The process according to claim 1271, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

1273. (NEW) The process according to claim 1272, wherein said fluorescent component comprises fluorescein.

1274. (NEW) The process according to claim 1249, wherein said A or Sig comprises a chemiluminescent component.

1275. (NEW) The process according to claim 1249, wherein said A or Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component.

1276. (NEW) The process according to claim 1249, wherein said A or Sig comprises an antibody component.

1277. (NEW) The process according to claim 1249, wherein said A or Sig comprises a chelating component.

1278. (NEW) The process according to claim 1177, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof.

1279. (NEW) The process according to claim 1177, wherein said A or Sig is detectable when it is attached to the nucleotide or nucleotide analog directly or through a linkage group.

1280. (NEW) The process according to claim 1279, wherein said linkage group does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal.

1281. (Twice Amended) The process according to claim 1177, wherein said detectable non-radioactive labeled nucleic acid fragment or fragments are terminally ligated or attached to a polypeptide.

1282. (NEW) The process according to claim 1281, wherein the polypeptide comprises a polylysine.

1283. (NEW) The process according to claim 1281, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin.

1284. (NEW) The process according to claim 1281, wherein said A or Sig comprises a ligand and the polypeptide comprises an antibody thereto.

1285. (NEW) The process according to claim 1177, wherein said separating step is carried out electrophoretically.

1286. (NEW) The process according to claim 1177, wherein said detecting step is carried out directly.

1287. (NEW) The process according to claim 1286, wherein said direct detection is carried out on one or more indicator molecules.

1288. (Amended) The process according to claim 1287, wherein said one or more indicator molecules comprise fluorescent nucleotides or nucleotide analogs.

1289. (Amended) The process according to claim 1288, wherein said fluorescent nucleotides or nucleotide analogs comprise fluorescent DNA.

1290. (NEW) The process according to claim 1177, wherein said detecting step is carried out by means of a directly detectable signal provided by said A or Sig detectable non-radioactive moiety.

1291. (Amended) The process according to claim 1290, wherein said detecting step the directly detectable signal providing A or Sig detectable non-radioactive moiety comprises a member selected from the group consisting of a fluorogenic compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound.

1292. (NEW) The process according to claim 1290, wherein said detecting step the directly detectable signal is provided by an enzyme.

1293. (NEW) The process according to claim 1177, wherein said detecting step is carried out by means of a indirectly detectable signal provided by said A or Sig detectable non-radioactive moiety.

1294. (NEW) The process according to claim 1293, wherein said detecting step the indirectly detectable signal is provided by a member selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme.

1296. (NEW) The process according to claim 1293, wherein said detecting step the indirectly detectable signal providing Sig detectable non-radioactive moiety comprises a compound capable of binding to an insoluble phase.

1297. (Twice Amended) The process according to claim 1177, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1298. (Twice Amended) A process for detecting a nucleic acid of interest in a sample, which process comprises the steps of:

(a) specifically hybridizing said nucleic acid of interest in the sample with one or more detectable non-radioactive labeled oligo- or polynucleotides, each such oligo- or polynucleotide being complementary to or capable of hybridizing with said nucleic acid of interest or a portion thereof, wherein said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

(ii) a nucleotide or nucleotide analog having the formula

Sig
|
PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

provided that when said nucleotide or nucleotide analog (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3′ position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3′ terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and

(b) detecting non-radioactively the presence of said Sig detectable non-radioactive moieties in any of the detectable non-radioactive labeled oligo- or polynucleotides which have hybridized to said nucleic acid of interest.

1299. (NEW) The process according to claim 1298, wherein the nucleic acid of interest comprises DNA, RNA or a DNA-RNA hybrid.

1300. (NEW) The process according to claim 1298, wherein the nucleic acid of interest is double-stranded or single-stranded.

1301. (NEW) The process according to claim 1298, wherein the nucleic acid of interest has been rendered single-stranded.

1302. (NEW) The process according to claim 1298, wherein the nucleic acid of interest is derived from an organism.

1303. (NEW) The process according to claim 1302, wherein the organism is selected from the group consisting of prokaryotes and eukaryotes.

1304. (Amended) The process according to claims 1302 or 1305, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing.

1305. (NEW) The process according to claim 1302, wherein said organism is living.

1306. (NEW) The process according to claim 1298, wherein the sample is suspected of containing an etiological agent and the nucleic acid of interest is naturally associated with the etiological agent.

1307. (NEW) The process according to claim 1306, wherein the sample is of human or animal origin and the etiological agent is selected from the group consisting of bacteria, virus and fungi.

1308. (NEW) The process according to claim 1298, wherein said nucleic acid of interest is derived from a member selected from the group consisting of *Streptococcus pyrogenes, Neisseria meningitidis, Staphylococcus aureus, Candida albicans, Pseudomonas aeruginosa, Neisseria gonorrhoeae, Mycobacterium tuberculosis*, and any combinations of the foregoing.

1309. (NEW) The process according to claim 1298, wherein said one or more oligo- or polynucleotides are derived from *Neisseria gonorrhoeae*.

1310. (NEW) The process according to claim 1298, wherein the sample comprises a bacterium suspected of containing a nucleic acid of interest which imparts resistance to an antibiotic and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the sequence of the bacterium which confers resistance to the antibiotic.

1311. (NEW) The process according to claim 1310, wherein when said bacterium is *Steptococcus pyrogenes* or *Neisseria meningtidis*, said antibiotic is penicillin, wherein when said bacterium is *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Streptococcus pyrogenes*, or *Neisseria gonorrhoeae*, said antibiotic is a tetracycline, and wherein when said bacterium is *Mycobacterium tuberculosis*, said antibiotic is an aminoglycoside.

1312. (NEW) The process according to claim 1311, wherein said bacterium is *Neisseria gonorrhoeae* and said antibiotic is selected from the group consisting of penicillin, tetracycline, aminoglycoside and combinations thereof.

1313. (NEW) The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid associated with the genetic disorder.

1314. (NEW) The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid of interest associated with thalassemia and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid which is absent in the thalassemic subjects.

1315. (NEW) The process according to claim 1298, wherein said process is utilized for chromosomal karyotyping which comprises contacting the sample with a series of the oligo- or polynucleotides which are complementary to a series of known genetic sequences located on chromosomes.

1316. (NEW) The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid which includes a terminal polynucleotide sequence poly A and wherein the oligo- or polynucleotide comprises a modified poly U molecule in which at least one uracil moiety has been modified by chemical addition of Sig to the 5' position of said uracil moiety.

1317. (NEW) The process according to claim 1298, wherein said process is utilized to determine the number of copies of an individual chromosome in a sample.

1318. (NEW) The process according to claim 1298, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme.

1319. (NEW) The process according to claim 1318, wherein said enzyme comprises terminal transferase.

1320. (NEW) The process according to claim 1298, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling.

1321. (Wholly Rewritten) The process according to claim 1320, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

1322. (NEW) The process according to claim 1320, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase.

1323. (NEW) The process according to claim 1298, wherein said incorporation comprises nick translation.

1324. (NEW) The process according to claim 1298 or 1323, wherein said incorporation is carried out by means of a polymerizing enzyme.

1325. (NEW) The process according to claim 1324, wherein said polymerizing enzyme comprises a polymerase.

1326. (NEW) The process according to claim 1325, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase.

1327. (NEW) The process according to claim 1298, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a monophosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate.

1328. (NEW) The process according to claim 1298, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate.

1329. (NEW) The process according to claim 1298, wherein said sugar moiety or sugar analog comprises a monosaccharide.

1330. (NEW) The process according to claim 1329, wherein said monosaccharide comprises a furanose.

1331. (NEW) The process according to claim 1330, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose.

1332. (NEW) The process according to claim 1298, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

1333. (NEW) The process according to claim 1298, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

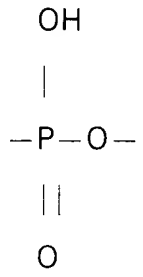
1334. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof.

1335. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N^4 position when said pyrimidine comprises cytosine, the N^2 position when said purine comprises adenine or deazaadenine, the N^6 position when said purine comprises guanine or deazaguanine, and combinations thereof.

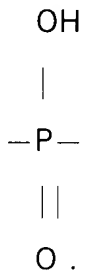
1336. (NEW) The process according to claim 1333, wherein in said nucleotide (ii), PM is attached to said monosaccharide or furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

1337. (NEW) The process according to claim 1333, wherein in said nucleotide (iii), PM is attached to said monosaccharide or furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said monosaccharide or furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

1338. (NEW) The process according to claim 1298, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



1339. (NEW) The process according to claim 1298, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig detectable non-radioactive moiety is covalently attached to PM through a phosphorus or phosphate oxygen.

1340. (Amended) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

1341. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

1342. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group.

1343. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

1344. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety.

1345. (NEW) The process according to claim 1298, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

1346. (NEW) The process according to claim 1345, wherein said linkage group contains an amine.

1347. (NEW) The process according to claim 1346, wherein said amine comprises a primary amine.

1348. (NEW) The process according to claim 1345, wherein said linkage group does not substantially interfere with nucleic acid hybridization or double-stranded nucleic acid formation.

1349. (Amended) The process according to claim 1345, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

1350. (NEW) The process according to claim 1298, wherein Sig comprises at least three carbon atoms.

1351. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

1352. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

1353. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

1354. (NEW) The process according to claim 1353, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

1355. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

1356. (NEW) The process according to claim 1355, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

1357. (NEW) The process according to claim 1298, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

1358. (Amended) The process according to claim 1298, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

1359. (NEW) The process according to claim 1358, wherein Sig comprises an electron dense component.

1360. (NEW) The process according to claim 1359, wherein said electron dense component comprises ferritin.

1361. (NEW) The process according to claim 1358, wherein Sig comprises a magnetic component.

1362. (NEW) The process according to claim 1361, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

1363. (NEW) The process according to claim 1361, wherein said magnetic component comprises magnetic beads.

1364. (NEW) The process according to claim 1298, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein.

1365. (NEW) The process according to claim 1364, wherein the binding protein comprises a lectin.

1366. (NEW) The process according to claim 1365, wherein the lectin comprises concanavalin A.

1367. (NEW) The process according to claim 1365, wherein said lectin is conjugated to ferritin.

1368. (NEW) The process according to claim 1358, wherein Sig comprises an enzyme.

1369. (NEW) The process according to claim 1368, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β-galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof.

1370. (NEW) The process according to claim 1358, wherein Sig comprises a hormone.

1371. (NEW) The process according to claim 1358, wherein Sig comprises a metal-containing component.

1372. (NEW) The process according to claim 1371, wherein said metal-containing component is catalytic.

1373. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule.

1374. (NEW) The process according to claim 1373, wherein said indicator molecule comprises an aromatic compound.

1375. (NEW) The process according to claim 1374, wherein said aromatic compound is heterocyclic.

1376. (NEW) The process according to claim 1375, wherein said heterocyclic aromatic compound is fluorescent.

1377. (NEW) The process according to claim 1376, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing.

1378. (NEW) The process according to claim 1377, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

1379. (NEW) The process according to claim 1358, wherein Sig comprises a fluorescent component.

1380. (NEW) The process according to claim 1379, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

1381. (NEW) The process according to claim 1380, wherein said fluorescent component comprises fluorescein.

1382. (NEW) The process according to claim 1358 wherein Sig comprises a chemiluminescent component.

1383. (NEW) The process according to claim 1358, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

1384. (NEW) The process according to claim 1358, wherein Sig comprises an antibody component.

1385. (NEW) The process according to claim 1358, wherein Sig comprises a chelating component.

1386. (Amended) The process according to claim 1373, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, and a chelating component, and a combination of any of the foregoing.

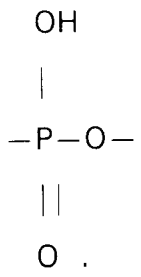
1387. (NEW) The process according to claim 1298, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof.

1388. (NEW) The process according to claim 1298, wherein Sig is detectable non-radioactively when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex.

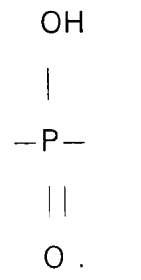
1389. (NEW) The process according to claim 1298, wherein Sig is detectable non-radioactively when it is attached to the nucleotide directly or through a linkage group.

1390. (NEW) The process according to claim 1389, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

1391. (NEW) The process according to claim 1298, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



1392. (NEW) The process according to claim 1298, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



1393. (Amended) The process according to claim 1298, wherein the oligo- or polynucleotide is terminally ligated or attached to a polypeptide.

1394. (NEW) The process according to claim 1298, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed.

1395. (NEW) The process according to claims 1393 or 1394, wherein the polypeptide comprises a polylysine.

1396. (NEW) The process according to claims 1393 or 1394, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin.

1397. (NEW) The process according to claim 1394, wherein Sig comprises a ligand and the polypeptide comprises an antibody thereto.

1398. (Amended) The process according to claim 1394, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

1399. (NEW) The process according to claim 1298, wherein said detecting step is carried out directly.

1400. (NEW) The process according to claim 1399, wherein said direct detection is carried out on one or more nucleotides or nucleotide analogs comprising indicator molecules.

1401. (Amended) The process according to claim 1400, wherein said one or more indicator molecules comprise fluorescent nucleotides or nucleotide analogs.

1402. (Amended) The process according to claim 1401, wherein said fluorescent nucleotides or nucleotide analogs comprise fluorescent DNA.

1403. (NEW) The process according to claim 1298, wherein said detecting step is carried out by means of a directly detectable non-radioactive signal provided by said Sig detectable non-radioactive moiety.

1404. (NEW) The process according to claim 1403, wherein said detecting step the directly detectable non-radioactive signal comprises a member selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound.

1405. (Amended) The process according to claim 1403, wherein said detecting step the directly detectable non-radioactive signal is provided by an enzyme.

1406. (NEW) The process according to claim 1298, wherein said detecting step is carried out by means of a indirectly detectable non-radioactive signal provided by said Sig detectable non-radioactive moiety.

1407. (NEW) The process according to claim 1406, wherein said detecting step the indirectly detectable non-radioactive signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme.

1409. (Twice Amended) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1410. (NEW) The process according to claim 1255, further comprising one or more washing steps.

1411. (Twice Amended) A process for detecting a nucleic acid of interest in a sample, which process comprises the steps of:

(A) providing:

(i) an oligo- or polynucleotide complementary to and capable of (1) specifically hybridizing to and forming a hybrid with a nucleic acid of interest or a portion thereof and (2) capable of binding to or complexing with a non-radioactively detectable protein; and

(ii) a non-radioactively detectable protein which is capable of binding to or complexing with said nucleic acid hybrid;

(B) contacting a sample suspected of containing said nucleic acid of interest with said oligo- or polynucleotide (i) and said non-radioactively detectable protein (ii) to form a complex; and

(C) detecting non-radioactively the presence of said non-radioactively detectable protein in said complex to detect said nucleic acid of interest.

1412. (NEW) The process according to claim 1411, wherein the nucleic acid of interest comprises DNA, RNA or a DNA-RNA hybrid.

1413. (NEW) The process according to claim 1411, wherein the nucleic acid of interest is double-stranded or single-stranded.

1414. (NEW) The process according to claim 1411, wherein the nucleic acid of interest has been rendered single-stranded.

1415. (NEW) The process according to claim 1411, wherein the nucleic acid of interest is derived from an organism.

1416. (NEW) The process according to claim 1415, wherein the living organism is selected from the group consisting of prokaryotes and eukaryotes.

1417. (Amended) The process according to claims 1415 or 1418, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing.

1418. (NEW) The process according to claim 1415, wherein said organism is living.

1419. (NEW) The process according to claim 1411, wherein the sample is suspected of containing an etiological agent and the nucleic acid of interest is naturally associated with the etiological agent.

1420. (NEW) The process according to claim 1419, wherein the sample is of human or animal origin and the etiological agent is selected from the group consisting of bacteria, virus and fungi.

1421. (NEW) The process according to claim 1411, wherein said nucleic acid of interest are derived from a member selected from the group consisting of *Streptococcus pyrogenes*, *Neisseria meningitides*, *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, *Mycobacterium tuberculosis*, and any combinations of the foregoing.

1422. (NEW) The process according to claim 1411, wherein said one or more oligo- or polynucleotides are derived from *Neisseria gonorrhoeae*.

1423. (NEW) The process according to claim 1411, wherein the sample comprises a bacterium suspected of containing a nucleic acid of interest which imparts resistance to an antibiotic and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the sequence of the bacterium which confers resistance to the antibiotic.

1424. (NEW) The process according to claim 1423, wherein when said bacterium is *Steptococcus pyrogenes* or *Neisseria meningtidis*, said antibiotic is penicillin, wherein when said bacterium is *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa, Streptococcus pyrogenes*, or *Neisseria gonorrhoea*, said antibiotic is a tetracycline, and wherein when said bacterium is *Mycobacterium tuberculosis*, said antibiotic is an aminoglycoside.

1425. (NEW) The process according to claim 1424, wherein said bacterium is *Neisseria gonorrhoeae* and said antibiotic is selected from the group consisting of penicillin, tetracycline, aminoglycoside and combinations thereof.

1426. (NEW) The process according to claim 1411, wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid associated with the genetic disorder.

1427. (NEW) The process according to claim 1411, wherein the sample is suspected of containing a nucleic acid of interest associated with thalassemia and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid which is absent in the thalassemic subjects.

1428. (NEW) The process according to claim 1411, wherein said process is utilized for chromosomal karyotyping which comprises contacting the sample with a series of the oligo- or polynucleotides (i) which are complementary to a series of known genetic sequences located on chromosomes.

1429. (NEW) The process according to claim 1411, wherein said process is utilized to determine the number of copies of an individual chromosome in a sample.

1430. (Twice Amended) The process according to claim 1411, wherein said non-radioactive detectable protein is selected from the group consisting of an antibody, a promoter, a repressor and an inducer.

1431. (NEW) The process according to claim 1430, wherein said repressor comprises a lac repressor.

1432. (Amended) The process according to claim 1430, wherein said at least one protein binding nucleic acid sequence is covalently attached to said oligo- or polynucleotide.

1433. (NEW) The process according to claim 1432, wherein said covalent attachment comprises ligation.

1434. (Amended) The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said non-radioactively detectable protein to bind to any hybrid formed between said oligo- or polynucleotide (i) and said nucleic acid of interest.

1435. (Amended) The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said non-radioactively detectable protein to be detected non-radioactively when bound to any hybrid formed between said oligo- or polynucleotide (i) and said nucleic acid of interest.

1436. (NEW) The process according to claim 1432, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a CH_2NH- moiety, or both.

1437. (NEW) The process according to claim 1436, wherein said covalent attachment comprises an allylamine group.

1438. (NEW) The process according to claim 1436, wherein said covalent attachment comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

1439. (NEW) The process according to claim 1432,wherein said covalent attachment includes a glycosidic linkage moiety.

1440. (NEW) The process according to claim 1432, wherein said protein binding sequence is covalently attached to any of the base, phosphate, or sugar moieties in said oligo- or polynucleotide.

1441. (NEW) The process according to claim 1440, wherein said covalent attachment is through a linkage group.

1442. (NEW) The process according to claim 1441, wherein said linkage group contains an amine.

1443. (NEW) The process according to claim 1442, wherein said amine comprises a primary amine.

1444. (NEW) The process according to claim 1441, wherein said linkage group does not substantially interfere with the binding of said non-radioactively detectable protein to said protein binding sequence.

1445. (NEW) The process according to claim 1411, wherein said non-radioactively detectable protein comprises a signaling component or indicator molecule.

1446. (NEW) The process according to claim 1445, wherein said signaling component or indicator molecule comprises at least three carbon atoms.

1447. (NEW) The process according to claim 1446, wherein said signaling component or indicator molecule comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

1448. (Amended) The process according to claim 1446, wherein said signaling component or indicator molecule comprises an aliphatic chemical moiety comprising at least four carbon atoms.

1449. (NEW) The process according to claim 1446, wherein said signaling component or indicator molecule comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

1450. (NEW) The process according to claim 1449, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

1451. (NEW) The process according to claim 1446, wherein said signaling component or indicator molecule comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

1452. (NEW) The process according to claim 1451, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

1453. (Amended) The process according to claim 1446, wherein said signaling component or indicator molecule comprises a monosaccharide, polysaccharide or an oligosaccharide.

1454. (Amended) The process according to claim 1445, wherein said signaling component or indicator molecule comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

1455. (NEW) The process according to claim 1445, wherein said signaling component or indicator molecule comprises an aromatic compound.

1456. (NEW) The process according to claim 1455, wherein said aromatic compound is heterocyclic.

1457. (NEW) The process according to claim 1456, wherein said heterocyclic aromatic compound is fluorescent.

1458. (NEW) The process according to claim 1457, wherein said fluorescent heterocyclic aromatic compounds is selected from the group consisting of fluorescein, rhodamine and dansyl.

1459. (NEW) The process according to claim 1458, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

1460. (NEW) The process according to claim 1454, wherein said signaling component or indicator molecule comprises a chemiluminescent component.

1461. (NEW) The process according to claim 1454, wherein said signaling component or indicator molecule comprises a chelating component.

1462. (NEW) The process according to claim 1411, wherein said non-radioactively detectable protein is detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof.

1463. (NEW) The process according to claim 1411, wherein said non-radioactively detectable protein is detectable when the oligo- or polynucleotide (i) is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex formed with said nucleic acid of interest.

1464. (NEW) The process according to claim 1411, wherein said nonradioactively detectable protein is detectable when it is attached to said oligo- or polynucleotide (i) directly or through a linkage group.

1465. (NEW) The process according to claim 1411, wherein said oligo- or polynucleotide (i) is contacted with said sample suspected of containing the nucleic acid of interest prior to forming a complex with said non-radioactively detectable protein.

1466. (NEW) The process according to claim 1411, wherein said detecting step is carried out directly.

1467. (NEW) The process according to claim 1466, wherein said direct detection of the non-radioactively detectable protein is carried out on one or more signaling components or indicator molecules.

1468. (Amended) The process according to claims 1467, wherein said direct detection step is carried out by a member selected from the group consisting of a fluorogenic compound, a chromogenic compound, a chemiluminescent compound, an enzyme, a radioactive compound and an electron dense compound.

1469. (NEW) The process according to claim 1411, wherein said detecting step is carried out indirectly.

1470. (Wholly Rewritten) The process according to claim 1469, wherein said indirect detection is carried out by a means selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a compound capable of binding to an insoluble phase, and a combination of any of the foregoing.

1471. (Twice Amended) The process according to claim 1411, wherein said nonradioactively detectable protein is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1472. (NEW) The process according to claim 1411, further comprising one or more washing steps.

1473. (Amended) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising the steps of:

contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

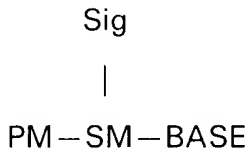
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety or an analog of any of the foregoing thereof, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

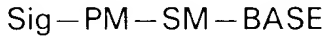
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group,

to permit specific hybridization of said clone or clones or DNA fragments or oligo- or polynucleotides to the locus or loci of said particular chromosome;

detecting non-radioactively any specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides, and determining the number of copies of said particular chromosome; and

comparing said determined number of copies of said particular chromosome with a number of copies of said particular chromosome determined for a normal cell containing said particular chromosome, and determining whether the number of copies of said particular chromosome in said cell is abnormal.

1474. (Amended) A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising the steps of:

providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

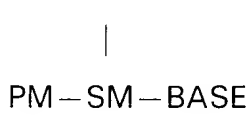
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

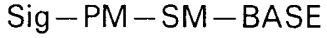
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set of clones or DNA fragments or oligo- or polynucleotides, permitting specific hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to said locus or loci in said chromosome of interest;

detecting non-radioactively any of said clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to said locus or loci in said chromosome of interest, and obtaining a pattern of hybridizations between said set of clones or DNA fragments or oligo- or polynucleotides and said chromosomes; and

identifying said chromosome of interest by means of said hybridization pattern obtained.

1475. (Amended) A process for identifying a plurality or all of the chromosomes in a cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein said clones or fragments or said oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci in a chromosome of said cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets are labeled with a different indicator molecule and each of said clones or DNA fragments or oligo- or polynucleotides comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotide or nucleotide analog are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

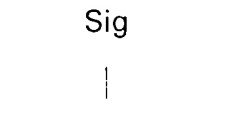
BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when

BASE is a pyrimidine or a pyrimidine analog, at a position other than the C8 position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

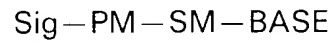
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to the locus or loci in said chromosomes; and

detecting non-radioactively any of said different indicator molecules in said sets of clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to the locus or loci in said chromosomes, and identifying any one of the chromosomes in said cell of interest.

1476. (Amended) A process for determining the number of chromosomes in an interphase cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments or oligo- or polynucleotides derived from said clones, wherein said set of clones or DNA fragments or oligo- or polynucleotides are specifically complementary to or specifically hybridizable with at least one locus or loci in a chromosome of said interphase cell of interest and each of said clones or DNA fragments or oligo- or polynucleotides in said sets comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

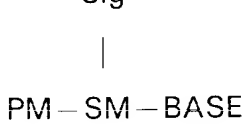
BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or a pyrimidine analog, at a position other than the C8

position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

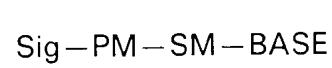
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is detectable non-radioactive moiety,

wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

contacting said interphase cell under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to any of the locus or loci in said chromosomes;

detecting non-radioactively any of said sets of clones or DNA fragments or oligo- or polynucleotides specifically hybridized to the locus or loci in said chromosomes, to obtain a pattern of generated signals; and comparing each generated signal with other generated signals in said pattern, and determining the number of chromosomes in said interphase cell of interest.

1477. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme.

1478. (NEW) The process according to claim 1477, wherein said enzyme comprises terminal transferase.

1479. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling.

1480. (Wholly Rewritten) The process according to claim 1479, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

1481. (NEW) The process according to claim 1479, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase.

1482. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation comprises nick translation.

1483. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation is carried out by means of a polymerizing enzyme.

1484. (NEW) The process according to claim 1483, wherein said polymerizing enzyme comprises a polymerase.

1485. (NEW) The process according to claim 1484, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase.

1486. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetraphosphate.

1487. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise nucleoside mono-, di- or tri-phosphate.

1488. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said sugar moiety or sugar analog comprises a monosaccharide.

1489. (NEW) The process according to claim 1488, wherein said monosaccharide comprises a furanose.

1490. (NEW) The process according to claim 1489, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose.

1491. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

1492. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing.

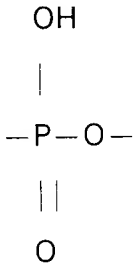
1493. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof.

1494. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N^4 position when said pyrimidine comprises cytosine, the N^2 position when said purine comprises adenine or deazaadenine, the N^6 position when said purine comprises guanine or deazaguanine, and combinations thereof.

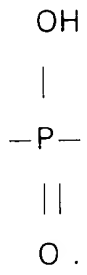
1495. (NEW) The process according to claim 1489, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

1496. (NEW) The process according to claim 1489, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

1497. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



1498. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen.

1499. (Amended) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

1500. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

1501. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group.

1502. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

1503. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety.

1504. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

1505. (NEW) The process according to claim 1504, wherein said linkage group contains an amine.

1506. (NEW) The process according to claim 1505, wherein said amine comprises a primary amine.

1507. (Amended) The process according to claim 1504, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

1508. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises at least three carbon atoms.

1509. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

1510. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

1511. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

1512. (NEW) The process according to claim 1511, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

1513. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

1514. (NEW) The process according to claim 1513, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

1515. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

1516. (Amended) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

1517. (NEW) The process according to claim 1516, wherein Sig comprises an electron dense component.

1518. (NEW) The process according to claim 1516, wherein said electron dense component comprises ferritin.

1519. (NEW) The process according to claim 1516, wherein Sig comprises a magnetic component.

1520. (NEW) The process according to claim 1519, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

1521. (NEW) The process according to claim 1519, wherein said magnetic component comprises magnetic beads.

1522. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a sugar residue and the sugar residue is completed with or attached to a sugar binding protein or a polysaccharide binding protein.

1523. (NEW) The process according to claim 1522, wherein the binding protein comprises a lectin.

1524. (NEW) The process according to claim 1523, wherein the lectin comprises concanavalin A.

1525. (NEW) The process according to claim 1523, wherein said lectin is conjugated to ferritin.

1526. (NEW) The process according to claim 1516, wherein Sig comprises an enzyme.

1527. (NEW) The process according to claim 1526, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof.

1528. (NEW) The process according to claim 1516, wherein Sig comprises a hormone.

1529. (NEW) The process according to claim 1516, wherein Sig comprises a metal-containing component.

1530. (NEW) The process according to claim 1529, wherein said metal-containing component is catalytic.

1531. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule.

1532. (NEW) The process according to claim 1531, wherein said indicator molecule comprises an aromatic compound.

1533. (NEW) The process according to claim 1532, wherein said aromatic compound is heterocyclic.

1534. (NEW) The process according to claim 1533, wherein said heterocyclic aromatic compound is fluorescent.

1535. (NEW) The process according to claim 1534, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing.

1536. (NEW) The process according to claim 1535, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

1537. (NEW) The process according to claim 1516, wherein Sig comprises a fluorescent component.

1538. (NEW) The process according to claim 1537, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

1539. (NEW) The process according to claim 1538, wherein said fluorescent component comprises fluorescein.

1540. (NEW) The process according to claim 1516, wherein Sig comprises a chemiluminescent component.

1541. (NEW) The process according to claim 1516, wherein Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component.

1542. (NEW) The process according to claim 1516, wherein Sig comprises an antibody component.

1543. (NEW) The process according to claim 1516, wherein Sig comprises a chelating component.

1544. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive. moiety comprises an indicator molecule.

1545. (Amended) The process according to claim 1544, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, and a chelating component, and a combination of any of the foregoing.

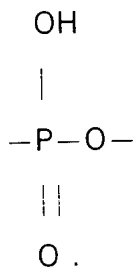
1546. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof.

1547. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is detectable when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex.

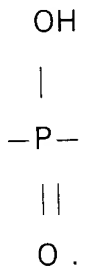
1548. (NEW) The process according to any of claims 1473, 1474,1475 or 1476, wherein Sig is detectable when it is attached to the nucleotide directly or through a linkage group.

1549. (NEW) The process according to claim 1548, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

1550. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



1551. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



1552. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein the oligo-or polynucleotide is terminally ligated or attached to a polypeptide.

1553. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed.

1554. (NEW) The process according to claim 1552, wherein the polypeptide comprises a polylysine.

1555. (NEW) The process according to claim 1553, wherein the polypeptide comprises a polylysine.

1556. (NEW) The process according to claim 1552, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin.

1557. (NEW) The process according to claim 1553, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin.

1558. (NEW) The process according to claim 1553, wherein Sig comprises a ligand and the polypeptide comprises an antibody thereto.

1559. (Amended) The process according to claim 1553, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

1560. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out directly.

1561. (NEW) The process according to claim 1560, wherein said direct detection is carried out on one or more indicator molecules.

1562. (Amended) The process according to claim 1561, wherein said one or more indicator molecules comprise fluorescent nucleotides.

1563. (Amended) The process according to claim 1562, wherein said fluorescent nucleotides or nucleotide analogs comprise fluorescent DNA.

1564. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of a directly detectable signal provided by said Sig detectable non-radioactive moiety.

1565. (Amended) The process according to claim 1564, wherein said detecting step is carried out by means of a member selected from the group consisting of a fluorogenic compound, a chromogenic compound, a cherniluminescent compound and an electron dense compound.

1566. (Amended) The process according to claim 1564, wherein said detecting step the directly detectable non-radioactive signal is provided by an enzyme.

1567. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of a indirectly detectable signal provided by said Sig detectable non-radioactive moiety.

1568. (NEW) The process according to claim 1567, wherein said detecting step the indirectly detectable non-radioactive signal is provided by a member selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme.

1570. (Twice Amended) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1571. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, further comprising one or more washing steps.

1572. (Wholly Rewritten) The process according to claim 1473, 1474, 1475 or 1476, wherein said one or more clones or DNA fragments or oligo- or polynucleotides derived from clone or clones are derived from said particular chromosome or said chromosome of interest or said chromosome in said interphase cell of interest.

1573. (Amended) The process according to claim 1475, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator molecule.

1574. (NEW) The process according to any of claims. 1473, 1474 or 1475, wherein said detecting step is carried out by a means selected from the group consisting of manual means and automatic means.

1575. (NEW) The process according to claim 1574, wherein said manual means comprises visualization.

1576. (NEW) The process according to claim 1574, wherein said automatic means comprises computerized automatic karyotyping.

1577. (NEW) The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator molecule.

1578. (NEW) The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with a different indicator molecule.

1579. (NEW) The process according to claim 1476, wherein said detecting and determining step is carried out by a means selected from the group consisting of manual means and automatic means.

1580. (NEW) The process according to claim 1579, wherein said manual means comprises visualization.

1581. (NEW) The process according to claim 1579, wherein said automatic means comprises computerized automatic karyotyping.

1582. (Twice Amended) A process for preparing a detectable non-radioactively labeled oligo- or polynucleotide of interest, comprising the steps of:

(A) providing either:

(1) one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA or an oligo- or polynucleotide of interest, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, wherein said other modified or unmodified nucleic acids are capable of incorporating into an oligo- or polynucleotide of interest, and wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs comprise one or more signaling moieties which are capable of providing directly or indirectly a detectable non-radioactive signal; or

(2) an oligo- or polynucleotide of interest comprising one or more said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides;

wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate moiety, the base moiety or the base analog, and are selected from the group consisting of:

(i)

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii)

Sig
|
PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety, and

wherein said PM is covalently attached to SM, said BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is detectable non-radioactive moiety; and

wherein PM is covalently attached to SM, BASE is covalently attached SM, and Sig is covalently attached to PM directly or through a linkage group;

provided that when said nucleotide or nucleotide analog (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3′ position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3′ terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and

said oligo- or polynucleotide of interest; and

(B) either incorporating said one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs (A)(1) into said oligo- or polynucleotide, and preparing a non-radioactive labeled oligo- or polynucleotide of interest, or preparing said oligo- or polynucleotide of interest from said oligo- or polynucleotide recited in step (A)(2) above.

1583. (NEW) The process according to claim 1582, wherein said oligo- or polynucleotide of interest is derived from an organism.

1584. (NEW) The process according to claim 1583, wherein said organism is living.

1585. (NEW) The process according to claims 1583 or 1584, wherein the organism is selected from the group consisting of prokaryotes and eukaryotes.

1586. (NEW) The process according to claim 1585, wherein said organism comprises a eukaryote.

1587. (NEW) The process according to claim 1586, wherein said eukaryotic oligo- or polynucleotide of interest is contained within a chromosome.

1588. (NEW) The process according to claim 1586, wherein said eukaryote comprises a mammal.

1589. (NEW) The process according to claim 1588, wherein said mammalian oligo- or polynucleotide of interest is contained within a chromosome.

1590. (NEW) The process according to claim 1588, wherein said mammal comprises a human being.

1591. (NEW) The process according to claim 1590, wherein said human oligo- or polynucleotide of interest is contained within a chromosome.

1592. (NEW) The process according to claim 1591, wherein said human chromosomal oligo- or polynucleotide of interest is part of a human gene library.

1593. (Amended) The process according to claims 1583 or 1584, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing.

1594. (NEW) The process according to claim 1584, wherein said living organism comprises a mammal.

1595. (NEW) The process according to claim 1594, wherein said mammal comprises a human being.

1596. (NEW) The process according to claim 1582, wherein said incorporating step is carried out using an enzyme.

1597. (NEW) The process according to claim 1596, wherein said enzyme comprises a polymerase.

1598. (NEW) The process according to claim 1597, wherein said polymerase comprises DNA polymerase.

1599. (Amended) The process according to claim 1582, wherein said nucleotide analog can be attached terminally to DNA or RNA by an enzyme.

1600. (NEW) The process according to claim 1599, wherein said enzyme comprises terminal transferase.

1601. (NEW) The process according to claim 1582, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling.

1602. (Wholly Rewritten) The process according to claim 1601, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

1603. (NEW) The process according to claim 1601, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase.

1604. (NEW) The process according to claim 1582, wherein said incorporation comprises nick translation.

1605. (NEW) The process according to claim 1582 or 1604, wherein said incorporation is carried out by means of a polymerizing enzyme.

1606. (NEW) The process according to claim 1605, wherein said polymerizing enzyme comprises a polymerase.

1607. (NEW) The process according to claim 1606, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase.

1608. (Amended) The process according to claim 1582, wherein said one or more detectable non-radioactive chemically modified nucleotides or said other modified or unmodified nucleic acids comprise a nucleoside di- or tri-phosphate.

1609. (NEW) The process according to claim 1582, wherein said incorporating step is template dependent or template independent.

1610. (NEW) The process according to claim 1609, wherein said incorporating step is template dependent.

1611. (Wholly Rewritten) The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest prepared by said incorporating step comprises at least one internal modified nucleotide.

1612. (NEW) The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest prepared by said incorporating step comprises at least one terminal modified nucleotide.

1614. (NEW) The process according to claim 1582, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a monophosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate.

1615. (NEW) The process according to claim 1582, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate.

1616. (NEW) The process according to claim 1582, wherein said sugar moiety or sugar analog comprises a monosaccharide.

1617. (NEW) The process according to claim 1616, wherein said monosaccharide comprises a furanose.

1618. (NEW) The process according to claim 1617, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose.

1619. (NEW) The process according to claim 1582, wherein in said chemically modified nucleotides or nucleotide analogs (i) Sig is covalently attached to said BASE at a position when BASE is a pyrimidine or pyrimidine analog that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine or purine analog that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof.

1620. (NEW) The process according to claim 1582, wherein in said chemically modified nucleotides or nucleotide analogs (i) Sig is covalently attached to said BASE at a position selected from the group consisting of the N^4 position when said pyrimidine or pyrimidine analog comprises cytosine or a cytosine analog, the N^2 position when said purine or purine analog comprises adenine, an adenine analog, or deazaadenine, the N^6 position when said purine comprises guanine or deazaguanine, and combinations thereof.

1621. (NEW) The process according to claim 1582, wherein said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) or both is selected from the group consisting of a pyrimidine, a pyrimidine analog, a purine, a purine analog, a 7-deazapurine, a 7-deazapurine analog, and a combination of any of the foregoing.

1622. (NEW) The process according to claim 1582, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) or both is selected from the group consisting of a pyrimidine, a pyrimidine analog, a purine, a purine analog, a 7-deazapurine, a 7-deazapurine analog, and a combination of any of the foregoing.

1623. (NEW) The process according to claim 1582, wherein in said incorporating step, Sig in the nucleotide (i) is covalently attached to BASE through a linkage group.

1624. (Amended) The process according to claim 1623, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

1625. (NEW) The process according to claim 1623, wherein said linkage group contains an amine.

1626. (NEW) The process according to claim 1625, wherein said amine comprises a primary amine.

1627. (NEW) The process according to claim 1582, wherein in said incorporating step, Sig in the nucleotide (ii) is covalently attached to SM through a linkage group.

1628. (Amended) The process according to claim 1627, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

1629. (NEW) The process according to claim 1627, wherein said linkage group contains an amine.

1630. (NEW) The process according to claim 1629, wherein said amine comprises a primary amine.

1631. (NEW) The process according to claim 1582, wherein in said incorporating step, Sig in the nucleotide (iii) is covalently attached to PM through a linkage group.

1632. (Amended) The process according to claim 1631, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

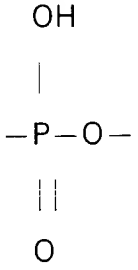
1633. (NEW) The process according to claim 1631, wherein said linkage group contains an amine.

1634. (NEW) The process according to claim 1633, wherein said amine comprises a primary amine.

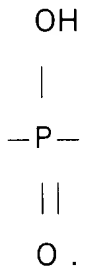
1635. (NEW) The process according to claim 1617, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or a pyrimidine analog, or the N9 position when BASE is a purine, a purine analog, 7-deazapurine, or a 7-deazapurine analog, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

1636. (NEW) The process according to claim 1617, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or a pyrimidine analog, or the N9 position when BASE is a purine, a purine analog, 7-deazapurine, or a 7-deazapurine analog, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

1637. (NEW) The process according to claim 1582, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



1638. (NEW) The process according to claim 1582, wherein PM is a mono-, di or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen.

1639. (Amended) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

1640. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α-position relative to the point of attachment to the nucleotide, a $-CH_2NH-$ moiety, or both.

1641. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group.

1642. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide, or any of the moieties

$$-CH = CH_2-NH- ,$$

$$-CH = CH-CH_2-NH- ,$$

$$-CH = CH-CH_2-O-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-NH- ,$$

$$-S- , \quad -\overset{\displaystyle O}{\overset{||}{C}}-O , \text{ and } -O- .$$

1643. (NEW) The process according to claim I582, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety.

1644. (NEW) The process according to claim 1582, wherein in said nucleotides or nucleotide analogs (i), (ii) or (iii), Sig is covalently attached to BASE, SM or PM through a linkage group.

1645. (NEW) The process according to claim 1644, wherein said linkage group contains an amine.

1646. (NEW) The process according to claim 1645, wherein said amine comprises a primary amine.

1647. (Amended) The process according to claim 1645, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

1648. (NEW) The process according to claim 1582, wherein said Sig comprises at least three carbon atoms.

1649. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

1650. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

1651. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

1652. (NEW) The process according to claim 1651, wherein said heterocyclic aromatic compound is fluorescent.

1653. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

1654. (NEW) The process according to claim 1653, wherein said heterocyclic aromatic compound is fluorescent.

1655. (NEW) The process according to claim 1582, wherein said Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

1656. (Amended) The process according to claim 1582, wherein said Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

1657. (NEW) The process according to claim 1656, wherein said Sig comprises an electron dense component.

1658. (NEW) The process according to claim 1657, wherein said electron dense component comprises ferritin.

1659. (NEW) The process according to claim 1656, wherein said Sig comprises a magnetic component.

1660. (NEW) The process according to claim 1659, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

1661. (NEW) The process according to claim 1659, wherein said magnetic component comprises magnetic beads.

1662. (NEW) The process according to claim 1582, wherein said Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein.

1663. (NEW) The process according to claim 1662, wherein the binding protein comprises a lectin.

1664. (NEW) The process according to claim 1663, wherein the lectin comprises concanavalin A.

1665. (NEW) The process according to claim 1663, wherein said lectin is conjugated to ferritin.

1666. (NEW) The process according to claim 1656, wherein said Sig comprises an enzyme.

1667. (NEW) The process according to claim 1666, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof.

1668. (NEW) The process according to claim 1656, wherein said Sig comprises a hormone.

1669. (NEW) The process according to claim 1656, wherein said Sig comprises a metal-containing component.

1670. (NEW) The process according to claim 1669, wherein said metal-containing component is catalytic.

1671. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule.

1672. (NEW) The process according to claim 1671, wherein said indicator molecule comprises an aromatic compound.

1673. (NEW) The process according to claim 1672, wherein said aromatic compound is heterocyclic.

1674. (NEW) The process according to claim 1673, wherein said heterocyclic aromatic compound is fluorescent.

1675. (NEW) The process according to claim 1674, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine and dansyl.

1676. (NEW) The process according to claim 1675, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein.

1677. (Amended) The process according to claim 1671, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chromogenic component, a chemiluminescent component, and a chelating component, and a combination of any of the foregoing.

1678. (NEW) The process according to claim 1656, wherein said Sig comprises a fluorescent component.

1679. (NEW) The process according to claim 1678, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl.

1680. (NEW) The process according to claim 1679, wherein said fluorescent component comprises fluorescein.

1681. (NEW) The process according to claim 1656, wherein said Sig comprises a chemiluminescent component.

1682. (NEW) The process according to claim 1656, wherein said Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component.

1683. (NEW) The process according to claim 1656, wherein said Sig comprises an antibody component.

1684. (NEW) The process according to claim 1656, wherein said Sig comprises a chelating component.

1685. (NEW) The process according to claim 1582, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof.

1686. (Amended) The process according to claim 1582, wherein said Sig is detectable non-radioactively when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex.

1687. (Amended) The process according to claim 1582, wherein said Sig is detectable non-radioactively when it is attached to the nucleotide directly or through a linkage group.

1688. (Amended) The process according to claim 1687, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

1689. (Wholly Rewritten) The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest is terminally ligated or attached to a polypeptide.

1690. (NEW) The process according to claim 1689, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed.

1691. (NEW) The process according to claim 1689, wherein the polypeptide comprises a polylysine.

1692. (NEW) The process according to claim 1689, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin.

1693. (Amended) The process according to claim 1690, wherein said Sig comprises a ligand and the polypeptide comprises an antibody thereto.

1694. (NEW) The process according to claim 1690, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chernilurninescent component, an antigen, a hapten, an antibody component and a chelating component.

1695. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is capable of being directly detected.

1696. (Amended) The process according to claim 1695, wherein said directly detectable signal providing Sig detectable non-radioactive moiety is selected from the group consisting of a fluorogenic compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound and an enzyme.

1697. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is capable of being indirectly detected.

1698. (Wholly Rewritten) The process according to claim 1697, wherein said detecting step the indirectly detectable signal is provided by a member selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme and a combination of any of the foregoing.

1699. (Twice Amended) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1700. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of chelating a metal or metal ion and providing a detectable signal, and wherein said one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting the presence of each of said separated or resolved fragments by means of the detectable signal provided by a metal or metal ion chelated by said chelating compounds or chelating components in the detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, and determining the sequence of said nucleic acid of interest.

1701. (Thrice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of chelating a metal or metal ion and providing a detectable signal, and wherein said one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

introducing or subjecting said fragments to a sequencing gel;

separating or resolving said fragments in said sequencing gel; and

detecting each of the separated or resolved fragments by means of the detectable signal provided by a metal or metal ion chelated by said chelating compounds or chelating components in the detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, and determining the sequence of said nucleic acid of interest.

1702. (Thrice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of chelating a metal or metal ion and providing a detectable signal, and wherein said one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof;

detecting with a sequencing gel the detectable non-radioactive labeled nucleic acid fragments by means of a metal or metal ion chelated by said chelating compounds or chelating components; and

determining the sequence of said nucleic acid of interest.

1703. (Thrice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the step of detecting with a sequencing gel one or more detectable non-radioactive labeled nucleic acid fragments comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of chelating a metal or metal ion and providing a detectable signal, and wherein said one or more detectable non-radioactive modified nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the base moiety or the base analog thereof.

1704. (Thrice Amended) A process for determining in a sequencing gel the presence of nucleic acid fragments comprising a sequence complementary to a nucleic acid sequence of interest or a portion thereof, said process comprising the steps of:

(A) providing

(i) one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into a nucleic acid, or

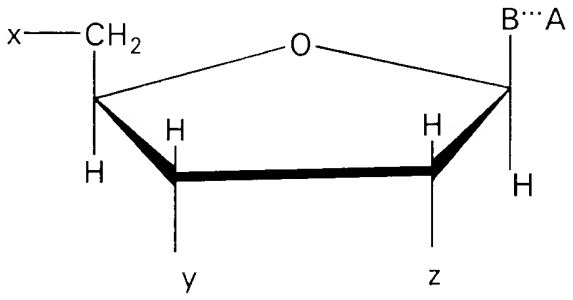
(ii) one or more oligonucleotides or polynucleotides comprising at least one of said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs; or

(iii) both (i) and (ii);

wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs (i) and said oligonucleotides and polynucleotides (ii) are capable of attaching to or coupling to or incorporating into or forming one or more nucleic acid fragments, wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of chelating a metal or metal ion and providing a detectable signal, and wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs have been modified non-disruptively or disruptively on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof; and;

(B) incorporating said one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs (i) or said one or more oligonucleotides or polynucleotides comprising at least one of said detectable non-radioactive chemically modified or labeled nucleotides (ii), or both (i) and (ii), into said one or more nucleic acid fragments, to prepare detectable non-radioactive labeled fragments, each such fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, said detectable non-radioactive labeled fragments further comprising one or more detectable non-radioactive chemically modified nucleotides or nucleotide analogs selected

from the group consisting of:

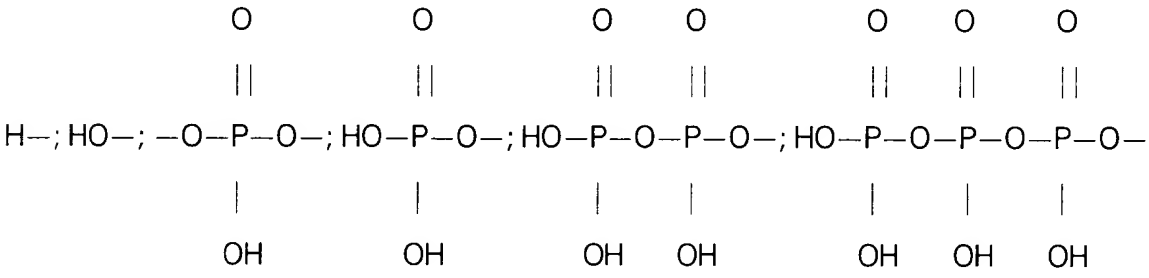


wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1'-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the, 7-deazapurine moiety or the 7-analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

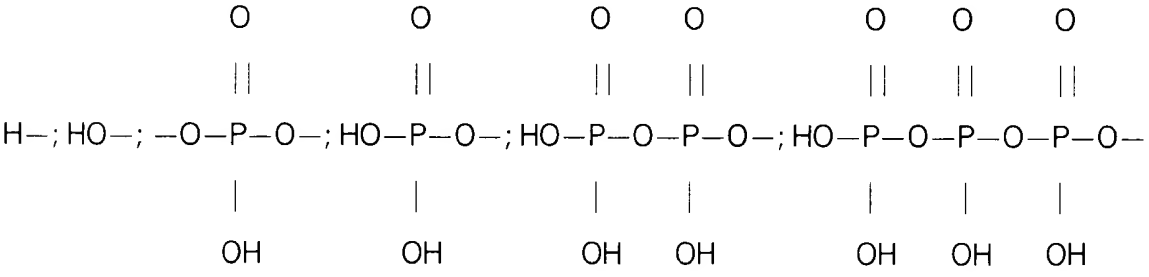
wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing directly or indirectly a detectable signal; and

wherein B and A are covalently attached directly or through a linkage group, and

wherein x comprises a member selected from the group consisting of:

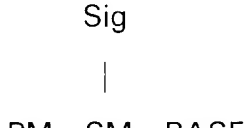


wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H- and HO-

(ii)



wherein

PM is a phosphate moiety or phosphate analog,

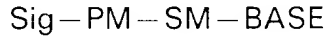
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, and

wherein said PM is covalently attached to SM, said BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog,

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal; and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

(C) transferring or subjecting said labeled fragments to a sequencing gel;

(D) separating or resolving said labeled fragments; and

(E) detecting directly or indirectly the presence of said labeled fragments by means of a metal or metal ion chelated by said chelating compounds or chelating components.

1705. (Twice Amended) A process for detecting a nucleic acid of interest in a sample, which process comprises the steps of:

(a) specifically hybridizing said nucleic acid of interest in the sample with one or more oligo- or polynucleotides, each such oligo- or polynucleotide being complementary to or capable of hybridizing with said nucleic acid of interest or a portion thereof, wherein said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety or a base analog of any of the foregoing; and

Sig is a signaling moiety comprising a chelating compound or component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

(ii) a nucleotide or nucleotide analog having the formula

Sig
|
PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or component capable of providing chelating a metal or metal ion and a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or components capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

provided that when said nucleotide or nucleotide analog (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3′ position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2', 3' vicinal

oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and

(b) detecting the presence of said signaling moieties Sig in any of the oligo- or polynucleotides which have hybridized to said nucleic acid of interest by means of a metal or metal ion chelated by said chelating compounds or chelating components.

1706. (Twice Amended) A process for detecting a nucleic acid of interest in a sample, which process comprises the steps of:

(A) providing:

(i) an oligo- or polynucleotide having two segments:

(a) a first segment complementary to and capable of hybridizing to a portion of said nucleic acid of interest; and

(b) a second segment comprising at least one protein binding sequence; and

(ii) a detectable protein capable of binding to said protein binding sequence and comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal;

(B) contacting a sample suspected of containing said nucleic acid of interest with said oligo- or polynucleotide (i) and said detectable protein (ii) to form a complex;

(C) detecting the presence of said protein in said complex and said nucleic acid of interest by means of a metal or metal ion chelated by said chelating compound or chelating component.

1707. (Thrice Amended) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising the steps of:

contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

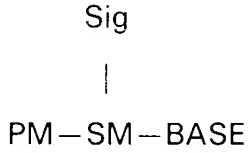
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety or an analog of any of the foregoing thereof, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5

position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

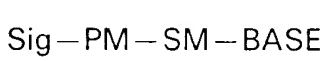
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, to permit specific hybridization of said clone or clones or DNA fragments or oligo- or polynucleotides to the locus or loci of said particular chromosome;

detecting the signal generated by said specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides by means of a metal or metal ion chelated by said chelating compound or chelating component, and determining the number of copies of said particular chromosome; and

comparing said determined number of copies of said particular chromosome with a number of copies of said particular chromosome determined for a normal cell containing said particular chromosome, and determining whether the number of copies of said particular chromosome in said cell is abnormal.

1708. (Twice Amended) A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising the steps of:

providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

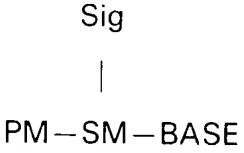
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position

other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

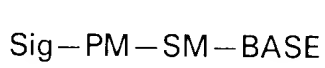
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set of clones or DNA fragments or oligo- or polynucleotides, permitting specific hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to said locus or loci in said chromosome of interest;

detecting by means of a metal or metal ion chelated by said chelating compound or chelating component any signal generated by each of said clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to said locus or loci in said chromosome of interest, and obtaining a pattern of hybridizations between said set of clones or DNA fragments or oligo- or polynucleotides and said chromosomes; and

identifying said chromosome of interest by means of said hybridization pattern obtained.

1709. (Twice Amended) A process for identifying a plurality or all of the chromosomes in a cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in a chromosome of said cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets are labeled with a different indicator molecule and each of said clones or DNA fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs capable of detection, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotide or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position

when BASE is a pyrimidine. or a pyrimidine analog, at a position other than the C8 position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog thereof;

(ii) a nucleotide or nucleotide analog having the formula

PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to the locus or loci in said chromosomes; and

detecting by means of a metal or metal ion chelated by said chelating compound or chelating component any signal generated by each of said different indicator molecules in said sets of clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to the locus or loci in said chromosomes, and identifying any one of the chromosomes in said cell of interest.

1710. (Twice Amended) A process for determining the number of chromosomes in an interphase cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically complementary to or specifically hybridizable with at least one locus or loci in a chromosome of said interphase cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotide or nucleotide analog are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

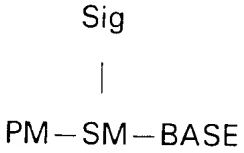
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a, pyrimidine moiety or a pyrimidine analog, at a position other than

the C8 position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog;

(ii) a nucleotide or nucleotide analog having the formula



wherein

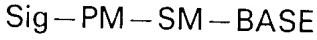
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

contacting said interphase cell under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to any of the locus or loci in said chromosomes;

detecting by means of a metal or metal ion chelated by said chelating compound or chelating component any signals generated by each of said sets of clones or DNA fragments or oligo- or polynucleotides specifically hybridized to the locus or loci in said chromosomes, to obtain a pattern of generated signals; and comparing each generated signal with other generate signals in said pattern, and determining the number of chromosomes in said interphase cell of interest.

1711. (Twice Amended) A process for preparing a labeled oligo- or polynucleotide of interest, comprising the steps of:

(A) providing either:

(1) one or more detectable chemically modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA or an oligo- or polynucleotide of interest, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, wherein said other modified or unmodified nucleic acids are capable of incorporating into an oligo- or polynucleotide of interest, and wherein said chemically modified or labeled nucleotides or nucleotide analogs comprise one or more signaling moieties comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, or

(2) an oligo- or polynucleotide of interest comprising one or more of said detectable chemically modified or labeled nucleotides or nucleotide analogs, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides,

wherein said chemically modified or labeled nucleotides or nucleotide analogs are modified on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog, and are selected from the group consisting of:

(i)

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii)

Sig
|
PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a signal, and wherein said PM is covalently attached to SM, said BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a metal or metal ion and providing a detectable signal; and wherein PM is covalently attached to SM, BASE is covalently attached SM, and Sig is covalently attached to PM directly or through a linkage group, provided that when said nucleotide or nucleotide analog (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3′ position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3′ terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and said oligo- or polynucleotide of interest; and

(B) either incorporating said one or more modified or labeled nucleotides or nucleotide analogs (A)(1) into said oligo- or polynucleotide, and preparing a labeled oligo- or polynucleotide of interest, or preparing said oligo- or polynucleotide of interest from said oligo- or polynucleotide recited in step (A)(2) above.

1712. (Amended) A process for detecting the presence of a nucleic acid of interest in a sample, comprising the steps of:

providing or generating (i) one or more detectable non-radioactively labeled oligonucleotides or polynucleotides, each of said detectable non-radioactively labeled oligonucleotides or polynucleotides comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to specifically hybridize therewith, wherein said one or more detectable non-radioactively labeled oligonucleotides or polynucleotides comprise one or more detectable non-radioactively modified or labeled nucleotides or nucleotide analogues, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactively modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof, and (ii) a sample that may contain said nucleic acid of interest;

forming in liquid phase hybrids comprising said one or more detectable non-radioactively labeled oligonucleotides or polynucleotides specifically hybridized with said nucleic acid of interest;

separating or resolving in a gel said formed hybrids; and

detecting non-radioactively the separated or resolved hybrids to detect the presence of said nucleic acid of interest.

1713. (NEW) The process according to claim 1712, wherein after said hybrid forming step, the liquid phase is subjected to nuclease treatment.

1714. (NEW) The process according to claim 1712, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA.

1715. (NEW) The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides are selected from the group consisting of DNA, RNA and DNA-RNA.

1716. (Amended) The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides comprise a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chromogenic component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component.

1717. (NEW) The process according to claim 1712, wherein said non-radioactive detection step is carried out directly or indirectly.

1718. (Twice Amended) The process according to claim 1712, wherein said detecting step is carried out by means of a member selected from the group consisting of enzymatic measurement, a fluorescent measurement, a chromogenic measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1719. (NEW) The process according to claim 569, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA.

1720. (NEW) The process according to claim 721, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA.

1721. (NEW) The process according to claim 873, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA.

1722. (NEW) The process according to claim 1025, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA.

1723. (NEW) The process according to any of claims 710, 862, 1014 or 1166, wherein said direct detection is carried out with the same indicator molecules.

1724. (NEW) The process according to any of claims 710, 862, 1014 or 1166, wherein said direct detection is carried out with different indicator molecules.

1725 (Amended) The process according to claim 1400, wherein said direct detection is carried out with the same indicator molecules.

1726. (Amended) The process according to claim 1400, wherein said direct detection is carried out with different indicator molecules.

1727. (NEW) The process according to claim 1712, wherein said detecting step comprises localizing said separated or resolved hybrids.

1728. (Twice Amended) The process of any of claims 1700, 1701, 1702 or 1704, wherein in said providing step, the chelating compounds or chelating components provide a detectable signal that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

1729. (Amended) The process of claim 1703, wherein said detecting step, the chelating compounds or chelating components provide a detectable signal that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminesscent, electron dense or magnetic.

1730 (Amended) The process of claim 1705, wherein said specific hybridizing step, the chelating compounds or chelating components provide a detectable signal that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

1731. (Amended) The process of claim 1707, wherein said contacting step, the chelating compounds or chelating components provide a detectable signal that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

1732. (Twice Amended) The process of any of claims 1700, 1701, 1702, 1703 or 1704, wherein said detecting step is carried out by a compound or component that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

1733. (Amended) The process of any of claims 1700, 1701, 1702, 1703 or 1704, wherein in said detecting step, the chelating compounds or chelating components have chelated a metal or metal ion selected from the group consisting of heavy metals and rare earth metals.

1734. (NEW) The process of claim 1733, wherein said heavy metal comprises cobalt.

1735. (NEW) The process of claim 1732, wherein said detecting step is carried out radioactively.

1736. (NEW) The process of claim 1735, wherein said radioactive detection is carried out by means of an isotope.

1737. (NEW) The process of claim 1736, wherein said isotope is a β or γ emitter.

1738. (NEW) The process of claim 1735, wherein said radioactive detection is carried out with an isotope selected from the group consisting of bismuth-206, bismuth-207, cobalt-60, gadolinium-153, strontium-90 and yttrium-90.

1739 (Amended) The process of any of claims 638, 640, 674, 676, 790, 792, 826, 828, 942, 944, 978, 980, 1094, 1096, 1130 or 1132, wherein said fluorescent aromatic or cycloaliphatic group comprises a fluorescent dye.

1740. (NEW) The process of any of claims 657, 693, 809, 845, 961, 997, 1113, 1149, or 1287, wherein said non-radioactively modified or labeled nucleotides or nucleotide analogs are labeled with the same indicator molecules.

1741. (NEW) The process of any of claims 657, 693, 809, 845, 961, 997, 1113, 1149, or 1287, wherein said non-radioactively modified or labeled nucleotides or nucleotide analogs are labeled with different indicator molecules.

1742. (NEW) The process of any of claims 583, 735, 887 or 1039, wherein said primers or said nucleoside triphosphates or analogs thereof are labeled.

1743. (Amended) The process of any of claims 569, 721, 873, 1025, 1177, 1700, 1701, 1702, 1703 or 1704, wherein said base analogs are selected from the group consisting of analogs of pyrimidine, purine and 7-deazapurine.

1744. (NEW) The process of claim 1743, wherein said purine analogs are selected from the group consisting of thymidine analogs, uridine analogs, deoxyuridine analogs, cytidine analogs and deoxycytidine analogs.

1745. (NEW) The process of claim 1744, wherein said uridine analogs comprise 5-bromo-2'-deoxyuridine-5'-phosphate.

1746. (NEW) The process of claim 1744, wherein said deoxycytidine analogs comprise 5-hydroxymethyl-2'-deoxycytidylic acid.

1747. (NEW) The process of claim 1743, wherein said purine analogs are selected from the group consisting of adenosine analogs, deoxyadenosine analogs, guanosine analogs and deoxyguanosine analogs.

1748. (NEW) The process of claim 1747, wherein said adenosine analogs are selected from the group consisting of tubericidin and toyocamycin.

1749. (NEW) The process of any of claims 1706, 1708, 1709, 1710 or 1711, wherein in said providing step, the chelating compounds or chelating components provide a detectable signal that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

1750. (NEW) The process of any of claims 1705, 1706, 1707, 1708, 1709, 1710 or 1711, wherein said detecting step is carried out by a compound or component that is radioactive, chromogenic, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

1751. (NEW) The process of any of claims 1705, 1706, 1707, 1708, 1709, 1710 or 1711, wherein in said detecting step, the chelating compounds or chelating components have chelated a metal or metal ion selected from the group consisting of heavy metals and rare earth metals.

1752. (NEW) The process of claim 1751, wherein said heavy metal comprises cobalt.

1753. (NEW) The process of claim 1750, wherein said detecting step is carried out radioactively.

1754. (NEW) The process of claim 1753, wherein said radioactive detection is carried out by means of an isotope.

1755. (NEW) The process of claim 1754, wherein said isotope is a β or γ emitter.

1756. (NEW) The process of claim 1753, wherein said radioactive detection is carried out with an isotope selected from the group consisting of bismuth-206, bismuth-207, cobalt-60, gadolinium-153, strontium-90 and yttrium-90.

1757. (NEW) The process of any of claims 1354, 1356, 1450, 1452, 1512, 1514, 1652 or 1654, wherein said fluorescent aromatic or cycloaliphatic group comprises a fluorescent dye.

1758. (NEW) The process of claims 1373 or 1671, wherein said non-radioactively modified or labeled nucleotides or nucleotide analogs are labeled with the same indicator molecules.

1759. (NEW) The process of claims 1373 or 1671, wherein said non-radioactively modified or labeled nucleotides or nucleotide analogs are labeled with different indicator molecules.

1760. (NEW) The process of any of claims 1298, 1473, 1474, 1475, 1476, 1582, 1705, 1706, 1707, 1708, 1709, 1710, 1711 or 1712, wherein said base analogs are selected from the group consisting of analogs of pyrimidine, purine and 7-deazapurine.

1761. (NEW) The process of claim 1760, wherein said purine analogs are selected from the group consisting of thymidine analogs, uridine analogs, deoxyuridine analogs, cytidine analogs and deoxycytidine analogs.

1762. (NEW) The process of claim 1761, wherein said uridine analogs comprise 5-bromo-2'-deoxyuridine-5'-phosphate.

1763. (NEW) The process of claim 1761, wherein said deoxycytidine analogs comprise 5-hydroxymethyl-2'-deoxycytidylic acid.

1764. (NEW) The process of claim 1760, wherein said purine analogs are selected from the group consisting of adenosine analogs, deoxyadenosine analogs, guanosine analogs and deoxyguanosine analogs.

1765. (NEW) The process of claim 1764, wherein said adenosine analogs are selected from the group consisting of tubericidin and toyocamycin.

1766. (NEW) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable non-radioactively labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactively modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA;

subjecting said detectable non-radioactively labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively the presence of each of said separated or resolved fragments by means of said detectable non-radioactively modified or labeled nucleotides or nucleotide analogs, and determining the sequence of said nucleic acid of interest.

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